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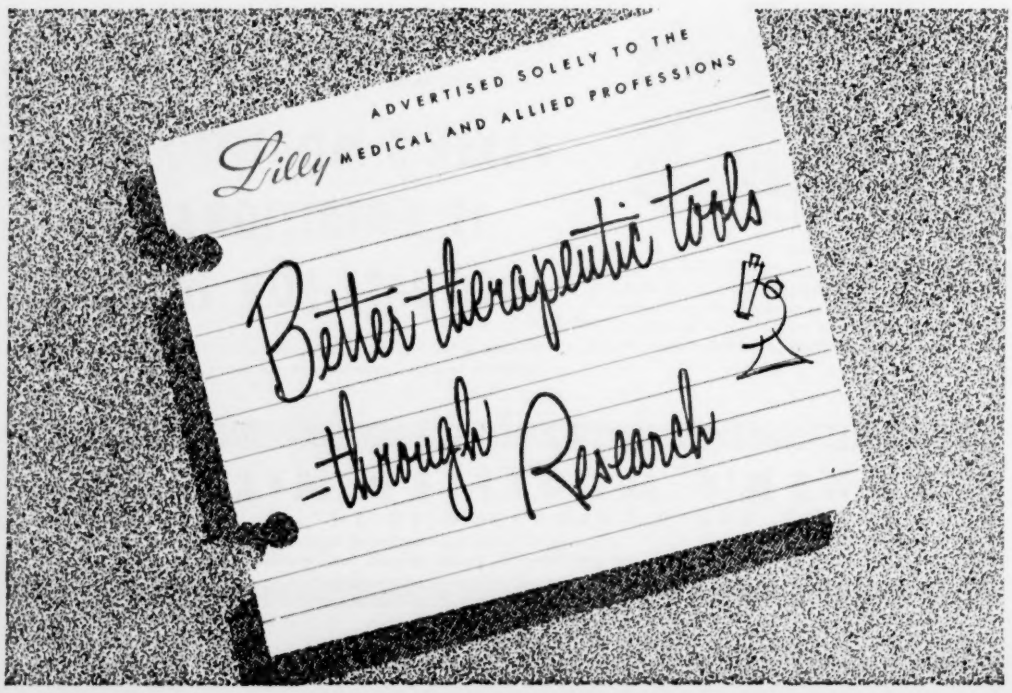

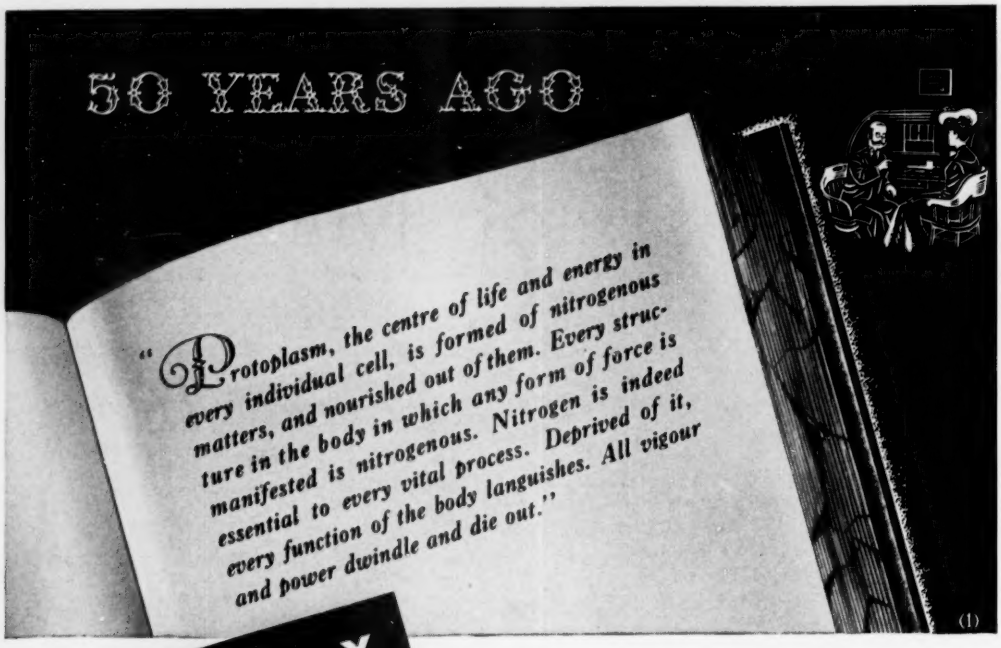
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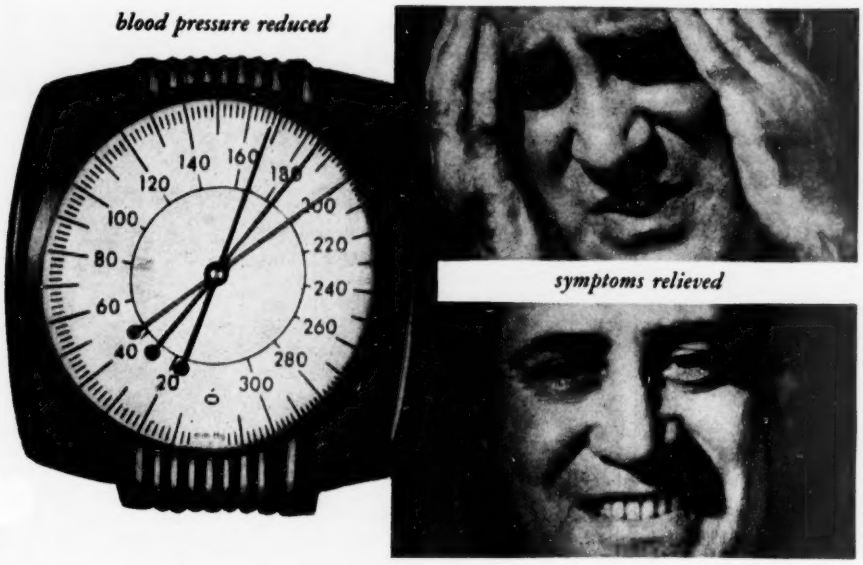

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1. Moyer, J. H., et al.: Am. J. M. Sc. *225*:379 (April) 1953.
2. Mills, L. C., and Moyer, J. H.: A.M.A. Arch. Int. Med. *90*:587 (Nov.) 1952.
3. Frankel, E.: Lancet *1*:408 (Feb. 17) 1951.
4. Johnson, L., et al.: Texas State J. M. *48*:331 (June) 1952.
5. Council on Pharmacy and Chemistry: J.A.M.A. *151*:585 (Jan. 31) 1953.
6. Grimson, K. S., et al.: J.A.M.A. *149*:215 (May 17) 1952.
7. Turner, R.: Lancet *1*:1217 (June 2) 1951.

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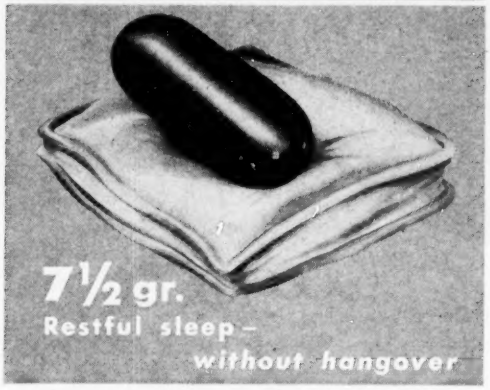

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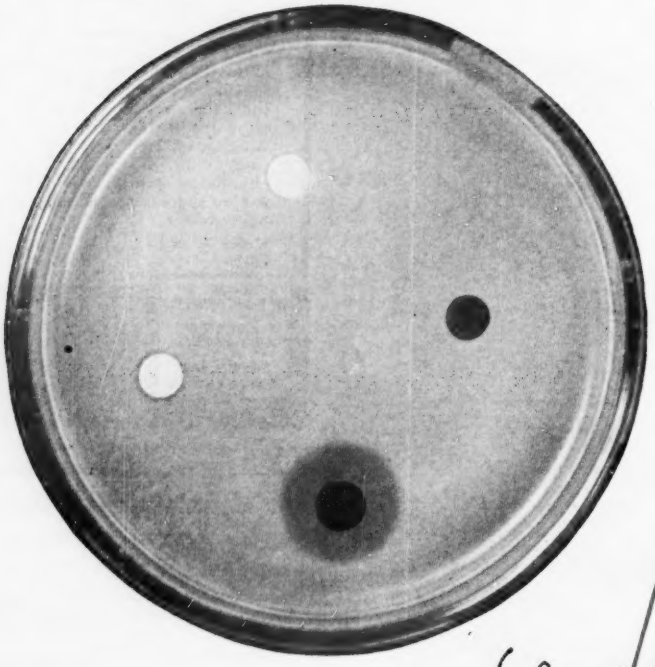

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1. Heller, E. M.: The Treatment of Essential Hypertension. *Canad. Med. Assn. Jour.*, 61:293, Sept., 1949.

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Volume 249 SEPTEMBER 24, 1953 Number 13

OBSERVATIONS ON NEOPLASTIC SPREAD*

Some Radiologic Aspects of the Problem

JOHN W. TURNER, M. D.†

SPRINGFIELD, MASSACHUSETTS

MANY patients with cancer have metastases when medical aid is first sought; in many others metastatic foci develop later. The earlier such metastases can be recognized, the greater the likelihood of significant palliation by application of the newer modes of therapy of the past two decades [1-5] and the improved older modes of treatment.[6-10]

Late symptoms produced by metastatic foci in organs and systems often remote from the primary site may lead patients to consult a neurologist, thoracic surgeon, orthopedist, internist or some other physician not involved in the earlier attempt to control the primary growth. Specialists in almost all fields of medicine and general practitioners can recall individual patients, often real diagnostic problems, whose complaints were eventually traced to metastatic neoplastic disease.

It has long been well established that tumor cells spread as emboli, cords or sheets along lymph and blood vessels, body spaces and tissue planes. One must be mindful of these basic facts and various ramifications of them to discover and distinguish metastatic extension from the great variety of malignant lesions to which mankind is subject.

Venous and lymphatic channels, with normally low pressures physiologically, are easily blocked, and this frequently predisposes to bizarre patterns of intercommunication. This fact alone accounts for many queerly distributed metastatic foci.

The intravenous injection of measured numbers of tumor cells into laboratory animals has provided helpful information about cell autolysis, dormancy and transpulmonary passage.[11] Such injection, with simultaneous withdrawal of aortic blood samples and recovery of the same tumor cells from animals, is interesting proof of the factor of transpulmonary passage in the spread of tumors. Warren and Gates[12] found that 11,000,000 tumor cells intravenously injected were necessary to induce growing foci in 100 per cent of the animals under study, and that the most important factor in the establishment of a metastatic focus was the growth potentiality of the individual cells selected.

Cancer spreads not only across body cavities and along tissue planes but also at times, avoidably or unavoidably, in the process of careful surgery.[13] Recurrences occur occasionally in scars even though the surgical technic has been good. Brandes, White and Sutton[14] report a case of recurrences in graft-donor sites of the thigh. In the course of an operation, a scirrhus carcinoma was found in the breast on biopsy, and the gloves and instruments were then discarded and new gloves and instruments employed for the radical mastectomy. The second gloves had been carefully washed in sterile distilled water before the grafts to cover the mastectomy defect were taken.

Martzloff and Manlove[15] have added a case report, making a total of 23 in the literature, in which cancer of the left kidney extended to the vagina and left ovary. This is based on venous communication proximally between the left renal and left ovarian veins and distally between the pampiniform plexus and uterovaginal venous plexus. In addition to the fact that cells frequently spread in bizarre patterns, it is of interest to note the reports of long-dormant states in the development of metastases. Cohen[16] reported a solitary pulmonary metastasis with bronchial involvement nine and a half years after resection of cancer of the colon. Solomon and Kreps[17] described liver involvement that on careful post-mortem study seemed to have arisen from a carcinoma of the sigmoid removed twenty-six years previously.

MATERIAL

For the past fifteen years, a standardized method has been used in the search for metastatic foci among patients at the Westfield State Sanatorium, Cancer Section. Films made are chosen to demonstrate the skull, spine, ribs and pelvis, the proximal portion of each femur and the lungs. On certain patients, serial surveys of this type have been recorded. At other times films are taken if there are symptoms or signs, as in extremities. Thus, an effort is made to

*From the Cancer Section, Westfield State Sanatorium, Massachusetts Department of Public Health.

†Radiologist, Tumor Section, Westfield State Sanatorium.

disclose metastatic foci clinically by survey of the lungs and major red bone-marrow areas.

Turner and Jaffe[18] reviewed a series of 1303 consecutive autopsies in 1940. Metastatic foci are listed in Table 1.

Continued interest in metastatic neoplasms has led to the presentation of this additional experience with emphasis on x-ray diagnostic signs. In this more recent experience at the Westfield State Sanatorium, Cancer Section, efforts have been made to check the reliability of various patterns of spread with autopsy material and other verified cases of cancer with extension beyond the primary site. It is not the purpose of this article to add to the excellent statistical data of Willis[19] and others,[20-22] but to emphasize observations that have seemed helpful in the clinical management of the patient with neoplastic disease. Particular reference is made to three general categories: metastases in lungs, in bones and in other structures such as the central nervous system, gastrointestinal tract and genitourinary tract. Statistical study in any such material as this is subject to many variables. Uniform clinical investigation of patients to theoretically adequate extents and correlation of all clinical findings with an extremely complete post-mortem examination of all suspected foci in all portions of the body exceed the bounds of practical realities. Even in teaching institutions and research hospitals these goals are never completely attained. Another discouraging statistical problem is the difficulty of collecting adequate statistically valid samples in all categories, even though a large patient series is under study.

Table 1. *Metastatic Foci Demonstrated in 1303 Autopsies.*

Organ and System	No. of Autopsies	Incidence of Metastasis	
		Bones	Lungs
		%	%
Glandular and hemopoietic	195	46.6	49.7
Urinary tract (male genitals)	185	36.7	28.1
Respiratory tract	96	13.5	28.1
Female genitals	160	6.2	23.1
Gastrointestinal tract	391	7.9	20.5
Oral cavity	218	1.8	11.9
Neuromuscular and skeletal	58	39.6	48.2
Total	1303		
Averages		18.4	26.6

With the recent trend to more and more radical surgical therapy of neoplastic disease and with the reservations concerning statistics already mentioned, we have been interested in a tabulation of the number of patients studied at autopsy with cancers still surgically resectable as judged by the pathological description of findings. It is of interest to note a relative parallelism between clinical results in malignant growths in different organs and the number of patients in these groups who have disease anatomically resectable by the most radical procedures now devised (Table 2). Expressed in another way, this distribution coincides with the frequently good results reported in various series of total laryngectomies or intensive radiotherapy of cancer of the larynx and the generally poor results reported in clinical series treated by resection for cancer of the body of the pancreas.

Skeletal Metastases

In clinical evaluation of bone lesions secondary to malignant tumors, the most consistent pattern in the material under consideration has been encountered in cancer of the prostate gland, in which the pattern of spread to the nearby bones is more prevalent than in any other primary cancer. The innominate bones, proximal femoral areas, sacrum, lower back and lower ribs in patient after patient are involved, in approximately that order. The relation of this cause and effect has been logically presented in carefully verified material by Warren et al.[23] Their explanation of spread by metastases through the rich regional perineural lymphatics seems more logical than that of the shunting of a small percentage of venous return from the prostatic area into the vertebral venous system at times of increased intra-abdominal pressure.[24-26] Since the larger percentage of the blood from the prostatic area returns through the caval system, even in Batson's[24-26] theory, one might properly expect more numerous remote bone metastases from the prostate than are found if prostatic cancer spread chiefly through the blood stream. The lack of a tendency for predominant vertebral or central-nervous-system distribution of metastases secondary to neoplastic disease of the testis likewise seems to imply a unique, though lesser, role for the vertebral veins as an incidental and not a major pathway for dissemination of tumor cells. The severe and early bone pain secondary to prostatic metastases seems additional evidence of predominant spread to involve sensory nerves and periosteum early through perineural lymphatic invasion rather than later through blood-borne emboli. In other words, extension to bone-marrow spaces seems to occur more frequently through the cortical ostia and inward, rather than by blood to the bone marrow and slowly outward through the cortex and finally to the sensitive periosteal covering. The distribution of pros-

Table 2. *Theoretical Resectability on the Basis of Post-Mortem Findings.*

Site of Cancer	Resectability
	%
Rectum	68.0
Endometrium	60.0
Colon	58.0
Larynx	57.0
Cervix	41.0
Stomach	17.0
Lungs	14.0
Pancreas	12.5

tatic metastatic foci in bone thus follows a more consistent and predictable pattern than foci from primary breast and renal cancers even though they too frequently spread to involve bone; metastases from these two organs show no overwhelming distribution in bones immediately adjacent to primary sites. The serum acid phosphatase level, if elevated, is helpful, though not always pathognomonic of prostatic metastases. This supplementary test is advocated in the patient with equivocal x-ray signs of metastatic disease from the prostate, or in follow-up study of the response of known metastases to therapy.

A useful observation concerning metastatic foci in bones, in our experience, has been frequent osteolytic but lack of osteoblastic foci from epidermoid carcinoma of the uterine cervix, the skin, the esophagus, the lungs and, in fact, all epidermoid carcinomas that have produced metastases, with the exception of a minority of bladder cancers. The rule that osteoblastic metastases are not from primary cancers that arise in stratified squamous epithelium is statistically safer than many rules in clinical usage.

My experience of the infrequent occurrence of metastatic foci in phalanges and other bones of the hands and feet parallels that of other observers.[27] In this series a renal-cell carcinoma metastasized to a distal phalanx of a middle digit in the right hand as a solitary osteolytic focus. Carcinoma of the thyroid gland metastasized to the fourth left toe, providing an additional example of osteolytic spread to an extremity.[28]

A problem in differential diagnosis was posed by a patient who had extensive Paget's disease with osteolytic foci in bones more suggestive of focal metastatic destructive change than of malignant transformation of Paget's disease. It was believed that radiologic differential diagnosis was uncertain. Biopsy revealed foci in two different bones to be secondary to cancer of the kidney, but growing in bone with x-ray and histologic findings typical of osteitis deformans.

The location and rate of growth of metastatic tissue has much to do with the determination of the film pattern produced. A primary malignant tumor of the retina in a two-year-old child metastasized to the ramus of a mandible and produced what has often been called a sun-ray effect. This film appearance, which has been observed more often in primary bone tumors, is occasionally seen in metastatic lesions.

Frequent localization of metastatic foci occurs in midshaft areas of long bones. Entry of a blood-borne embolus through the nutrient artery seems a logical explanation for such a solitary focus. In recent years patients with fractures from these lesions have been made more comfortable by intramedullary rod fixation in addition to the usual therapeutic measures, such as deep x-ray therapy and, if the extension is from a sex-associated primary cancer, appropriate hormonal alteration by radiation, surgery or drugs, or a combination of these.

Patients with cancer, particularly women after the menopause, are likely to be elderly and osteoporotic. Sometimes, it is difficult to determine whether vertebral bodies are collapsed because of this osteoporosis or from metastatic invasion or both. The tendency for relatively orderly, symmetrical, uniform collapse in osteoporosis and for uneven collapse in vertebral bodies involved by cancer is a helpful differential point when decalcification is so extensive as to obscure the bone detail on films.

Another anatomic consideration that has long been recognized and that we have frequently observed is the tendency for cartilage in joints, as elsewhere, to serve as a fairly effective barrier against neoplastic spread. Long-term preservation of the joint proper often occurs despite adjacent destructive change in bone.

I have observed the typical changes of leukemia in bones of children, but only rarely in adults. One such exception was recorded in a patient who had been under treatment for chronic myelogenous leukemia at intervals for eight years when bone pain developed. Films revealed small, scattered osteolytic foci in the bones of the pelvis and in each femur. Several other adult patients afflicted with chronic leukemia and similar bone pain did not have such x-ray signs.

A practical clinical correlation in patients who have metastatic involvement of the outer table of the skull, particularly from cancer of the breast, is the association of palpable elevations over the scalp. Sometimes, these are noted by the patient, but they are often discovered at physical examination in the follow-up clinic by palpation of the scalp. Frequently, such a palpable nodule facilitates the differential diagnosis of radiolucent foci in the cranial vault.

As examples of the broad variety of bone metastases, the following are mentioned: a neoplastic fracture through an osteolytic focus secondary to cancer of the cervix was found in a left femoral stump (amputation was done early in life for an injury); a twenty-three-year-old man had a neoplastic fracture of the right tenth rib secondary to carcinoma simplex of the stomach; and detachment of the lesser trochanter of the left femur occurred secondary to an osteolytic metastatic lesion from an epidermoid carcinoma of the esophagus.

A functioning thyroid metastatic focus in the upper left thoracic area was accompanied by the classic clinical picture of hyperthyroidism even after thyroidectomy. Biopsy from the chest wall revealed a histologic appearance indistinguishable from that of normal thyroid tissue (formerly called "benign metastasizing goiter"). One may expect this type of metastatic lesion to be among the 15 to 20 per cent

of thyroid cancers that respond favorably to radioiodine therapy.

Some physicians view the probability of spread from certain primary cancers to bones with incredulity, but such an attitude is scarcely justifiable, for, on occasions, almost any primary malignant growth may metastasize to almost any bone. From primary cancers of the lip, in this series, there was a case of metastatic involvement of a left rib, as well as one of spread to invade the middle cranial fossa.

Intrathoracic Involvement

Spread of cancer to lungs, pleura, pericardium, heart and hilar and mediastinal lymph nodes and various combinations of these sites produces a variety of x-ray appearances that may simulate many non-neoplastic conditions. Prevalent patterns include the tendency for cancer of the breast to spread by direct extension to the pleura of the same side of the chest and to produce pleural effusion and further dissemination in this manner. It is relatively common for a miliary type of lung dissemination to occur from primary cancer of the stomach or pancreas.

One occasionally sees numerous metastatic foci in both lungs under circumstances that suggest entry of a large number of tumor cells directly into the blood stream. Such an example in our group was encountered in an aged man with an advanced epidermoid, Grade 2 primary cancer of the tongue. Literally hundreds of nodules appeared in all lobes of both lungs and grew steadily. Two similar extremely disseminated cases of pulmonary involvement were secondary to sarcoma of the uterus in premenopausal patients. Such foci from primary cancers located in vascular, muscular, active organs suggest the possibility of unusually free entry of tumor cells into veins in occasional cases.

Calcium has been reported in various metastatic lesions.[29, 30] I have observed a number of patients in whom calcium was produced in the metastatic foci, coinciding with osteogenic, sarcomatous, primary growths. The irregular nature of the deposition of the calcium frequently helps differentiate these foci from calcium likely to be of more orderly arrangement if secondary to chronic inflammatory disease.

X-ray films of the chest often suggest invasion of the phrenic nerve by neoplastic disease and elevation of the corresponding side of the diaphragm, subject to verification by fluoroscopic observation.[31] In addition to this complication from primary carcinoma of the lung, I have seen it repeatedly from metastatic foci placed high and medially in the chest or anterior to the hilus and growing adjacent to the phrenic nerve in an invasive manner.

In years past, a prevalent clinical opinion about metastatic disease was that hemoptysis was infrequent. In more recent experience, I have seen several cases of hemoptysis in conditions besides metastatic chorionepithelioma. Lung metastases secondary to cancer of the colon and pulmonary foci of lymphoma have been among the more frequent causes of hemoptysis of this type. In 1 case, twenty-six months after resection of a carcinoma of the rectum copious hemoptysis, which proved to be of nearly fatal proportions, developed and was found to emanate from a solitary metastatic lesion in the lingula. Palliative resection was done, and the subsequent course continues to be favorable. A focus of metastatic adenocarcinoma from the sigmoid to the right upper lobe had the complication of central necrosis and abscess formation. This tendency for bleeding and communication with bronchi coincides with the increasing frequency of reports of metastatic cells found in the sputum or in specimens obtained by bronchoscopic aspiration.[32]

Among patients with chorionepithelioma, 3 in whom disseminated pulmonary lesions developed had hemoptysis of variable amounts and died in spite of various forms of treatment. A fourth, who had disseminated metastatic foci, has shown steady reduction in prominence of these foci and has improved in general condition, after panhysterectomy without supplementary radiation or hormone therapy.

If a metastatic focus originates near a larger bronchus and grows expansively, it may produce complete atelectasis of a lung or of a complete lobe, as in a patient whose primary growth was a hemangioendothelioma of the right thigh and whose metastatic focus was so placed adjacent to the left main bronchus as to cause complete atelectasis of the lung. Another patient, with a fibrosarcoma of the left forearm, had a metastatic focus in the right hilar area and had occlusion of the right main bronchus, with complete atelectasis of the right lung.

I have observed 2 malignant lesions of the adrenal gland, 1 of which was a malignant pheochromocytoma similar to that described by Cross and Pace.[33] Extensive involvement of the mediastinal lymph nodes and metastases to the right lung, superior vena cava and right atrium were noted, with phrenic-nerve paralysis secondary to metastatic invasion as well. Another primary adrenal cancer, which was regarded as of cortical origin, produced a large metastatic mass in the superior mediastinum in the region of the aortic arch that simulated an aneurysm.

On rare occasions, the differential diagnosis of pulmonary masses has been aided by the evaluation of homogeneity of a pulmonary soft-tissue deposit. Sarcomatous foci are likely to be very homogeneous, in contrast to the less homogeneous appearance of epithelial cancer. It is not possible to place complete reliance on this differential point, which should be employed as an additional helpful clue if the homogeneity or lack of homogeneity is quite definite.

Pulmonary osteoarthropathy has been reported from primary neoplastic involvement of the lung.[34]

Its occurrence with symptoms of joint pain may be confusing and may simulate chronic arthritis. A patient with metastatic malignant melanoma showed a rapid increase in typical clinical and x-ray signs of pulmonary osteoarthropathy, which subsided after palliative excision of the right lung for metastatic disease near the right hilus.

As an example of limitations in lung survey, a male patient with malignant melanoma who has been under observation for thirteen years had an initially inoperable lesion in the left inguinal area, verified by biopsy and partial excision. This lesion responded to radiation therapy, and the patient remained well until eight years later. At that time, a metastatic lymph node recovered from the medial right supraclavicular area proved to be malignant melanoma. The chest has remained normal on repeated radiograms throughout the interval of observation. The presence of a normal chest film in a patient with this particular anatomic distribution of disease leads us to believe that intermediately placed malignant cells are dormant, or that this represents a most unusual example of intercommunication of lymphatic extension.

Involvement of the heart and pericardium[35-37] is frequently detected at post-mortem investigation. In a group of 385 consecutive autopsies in this series, 12 cases of such involvement were recorded. Clinical and radiologic recognition of this complication, which lags far behind autopsy incidence, is based principally on the accumulation of pericardial fluid, which may or may not be a striking feature. Incidentally, in the same series, 11 patients had metastatic foci in the spleen.

Two groups of primary neoplasms that arise within the thorax — namely, those of lungs and those of esophagus — were associated with a discouragingly high incidence of metastasis, as demonstrated by McCort and Robbins.[38] Their findings should be helpful in the evaluation of operable patients and in the follow-up care of patients with such disease. I have found the administration of barium and the employment of the esophagus as a guide to metastatic lymph nodes helpful. Angiocardiography is similarly helpful, principally in our experience from alteration of the larger veins in the upper mediastinal area secondary to such extension. Steinberg and his associates[39] have summarized this method of investigation on the basis of venous and arterial distortion by adjacent neoplastic extension.

Soft-Tissue Changes

In recent years, greater reliance has been placed on contrast mediums for the evaluation of the urinary tract and the gastrointestinal tract so far as signs of spread to retroperitoneal lymph nodes are concerned.

The feature that I have found most helpful in evaluation of spread as it encroaches upon the gastrointestinal tract is the extrinsic appearance of the defect. A practically complete obstruction of the third portion of the duodenum was demonstrated in a patient known to have a malignant primary lesion of the prostate. The lesion did not seem intrinsic to the mucosa of the duodenum, and the defect was quite long. Palliative surgery revealed an adenocarcinoma consistent with origin in the prostate gland, metastatic to upper retroperitoneal lymph nodes so situated as to encroach upon the third portion of the duodenum. Similarly, a patient known to have had a primary duct-cell carcinoma of the breast who was being followed manifested symptoms of large-bowel obstruction. Barium-enema examination revealed an elongated defect, of extrinsic type, in the right half of the transverse colon. Operation and biopsy showed tissue that, in the opinion of the pathologist, could not have arisen in the colon and was entirely consistent with a duct-cell primary cancer of the breast. A similar problem has occurred from time to time in patients with various forms of lymphoma, which seems frequently to involve lymph nodes near the stomach, small bowel or colon, and secondarily to encroach on these structures, producing bizarre patterns of distortion and sometimes secondary mucosal ulceration. Metastatic lymph nodes in the upper abdomen as from breast cancer have caused displacement of the duodenum and distal portion of the stomach in a distinctive manner, best demonstrated in straight lateral projections after ingestion of barium.

In connection with the urinary tract, it is well established that ureteral distortion is a good method for evaluation of retroperitoneal lymph-node extension secondary to testicular cancer, verified examples having been encountered frequently in this series. A thirty-two-year-old woman with a malignant dysgerminoma of the ovary had an irregular mass as a postoperative recurrence that caused a large imprint on the bladder dome, with lateral displacement of the neighboring distal ureter. Such indirect evidence is, of course, even more commonly employed in the evaluation of uterine cancer, particularly in carcinoma of the cervix, with extension to the ureters. About a third of the patients seen at this hospital have significant ureteral involvement at the time of the excretory urogram on admission.

Metastases involving the nervous system[40, 41] may lead to the development of paraplegia. This is frequently related to obvious adjacent vertebral disease, usually with a neoplastic fracture as a complication. On the other hand, the disease may be first manifested by severe pain or paraplegia without a bone lesion. A patient with chorionepithelioma had such a complication as one of the terminal manifestations of her disease. The evaluation of epidural nodules merits more frequent employment of myelography, as recommended by Epstein.[42] This also has the tactical advantage of a definite

localization of the tumor for palliative radiation therapy. Another type of lesion of the central nervous system, in our series, occurred in a patient who was first treated for inoperable carcinoma of the cervix, with extensive invasion, with induration and edema, of the vaginal vault and most of the vaginal wall. The response to radiotherapy was both gratifying and surprising, and the originally positive biopsy was reversed by this therapeutic effect. Four years later, this patient entered the hospital with the symptoms of tumor of the right frontal lobe, which was demonstrated by cerebral angiography as a soft-tissue mass in the frontal-lobe area. Resection of this mass, which seemed to represent a solitary focus, revealed a tissue type consistent with that of the original primary uterine lesion. Since there was no evidence of involvement of lungs or bones, this may have represented dissemination through the vertebral venous system.

A more common experience[43] is the extension of cancer of the lung to the brain, frequently simulating a primary brain tumor, and occurring with such regularity as to lend support to the theory of predilection of lung cancer for localization in brain tissue.

Differential Diagnosis

Some of the more common and practical points in differential diagnosis encountered in the management of patients with cancer include the differentiation of osteoblastic disease from the prostate, as one possibility, and Paget's disease, particularly in the early or atypical form, as another, or, rarely, recognition of a combination of the two. Ordinarily, the uniformity of disease throughout a bone in osteitis deformans is quite distinctive. It is here that the elevated serum acid phosphatase may be helpful since such a chemical change does not occur in Paget's disease, although the serum alkaline phosphatase may be elevated with either Paget's disease or prostatic metastases.

A specific problem of distinguishing metastatic cancer localizing on the periosteal aspect of a femoral shaft from fibrosarcoma encroaching on the femur in a similar manner was difficult to evaluate, and from the x-ray signs the only diagnosis offered was that of cancer. Biopsy revealed an atypical form of thyroid cancer without appreciable cortical destruction but with periosteal stimulation to form an irregular sun-ray appearance in a bulky lesion, chiefly of soft-tissue density.

A large mucocele of the sphenoid sinus eroded neighboring bone in such a way as to simulate irregular extension of cancer from the nasopharynx into the middle cranial fossa.

A patient who had received an intrapleural injection of foreign material in the therapy of tuberculosis showed unusual rounded densities after an interval of twenty-eight years. These simulated metastatic lesions until carefully evaluated with the knowledge of the history. The shadows were produced by multifocal encapsulation of the injected material.

Radiation pleuropulmonitis may simulate metastatic disease, depending on the phase of the process. Usually, correlation with the amount, location and sequence of treatment suffices for the differential diagnosis.

Osteitis pubis may resemble osteolytic metastatic involvement in the region of one or both pubic bones at the symphysis, but this can usually be evaluated by a combination of clinical observation and serial x-ray studies.

Osteitis condensans ilii[44] may reproduce the picture of osteoblastic metastatic involvement of the posterior portion of one or both iliac bones but usually occurs in young female patients of adult age, and seems to recede spontaneously.

Some unusual inflammatory lesions, such as coccidioidomycotic nodules, may simulate metastatic foci,[45] but these patients, when questioned, are likely to know of a geographic contact in an area where the disease is endemic. Coccidioidin skin testing is relatively effective in evaluation of such suspects.

Palliative Resection

One of the most important contributions of recent years has been the application of surgical therapy for solitary metastatic nodules. The radiologist should make every effort to evaluate patients for this possible mode of therapy. My experience indicates that the following criteria might well be applied:

The primary growth should be controlled; the longer and more complete the control, the more favorable the prognosis for palliative resection of a solitary lesion.

The primary lesion should be a well differentiated tissue type; the more complete the histologic differentiation, the more favorable the prognosis.

The duration from the time of control of the primary growth to the first recognition of the metastatic focus should be greater than a year; in fact, the longer the interval beyond that period, the more favorable the prognosis.

I have observed highly worthwhile palliative resection of pulmonary metastatic foci secondary to osteogenic sarcoma, rectal neoplasm, cancer of the transverse colon, malignant lesions of the uterus and others. Reyes and Horrax[46] reported in 1950 on resection of a metastatic cerebral focus from malignant melanoma. This patient is still living and well eight years after operation.

For localized metastatic disease not amenable to surgery, utilization of intensive radiotherapy is all the more indicated. In our clinical material we have as examples of this a four-year survival after metastatic involvement from breast cancer with metastatic collapse of a vertebral body, and a six-year

survival after metastatic involvement of both lungs that became evident eight years after hysterectomy for endometrial adenocarcinoma. Each of the last 2 patients was treated by radiotherapy alone. In more recent years the combination of hormone-level alteration with radiotherapy has made such experiences in the control of these metastases commonplace.

Summary and Conclusions

Metastatic extension of neoplastic disease should be recognized as early as possible, that the patient may have the increasing benefits of improved and newer modes of therapy. The practical value of such therapeutic measures compares favorably with that of treatment offered patients suffering from serious chronic, non-neoplastic disease. Various clinical experiences are mentioned in support of these contentions.

Physicians should abandon the thought that certain cancers are not expected to spread to the lungs or to the bones, and replace it with a program of radiographic surveying of lungs and major red bone-marrow areas for cancers with a high metastatic index, such as those of the breast, prostate, kidney, lung, thyroid gland, bones or testicles. In addition, there should be a policy of x-ray investigation of atypical symptoms referable to lungs, skeleton, central nervous system or intestinal and urinary tracts in the clinical follow-up study of all patients with neoplastic disease.

In my experience, relatively early widespread metastatic disease from cancer of the lungs, stomach and pancreas coincides with disappointing results from radical surgery of these lesions. Still earlier diagnosis of these primary cancers remains essential. On the other hand, a tendency for cancers of the larynx, colon, rectum, uterine fundus and, to a lesser degree, uterine cervix to remain anatomically resectable longer coincides with relatively good percentages of five-year survivals in these conditions. One gains the impression, from a combination of autopsy and clinical follow-up study, that cancer of the oral cavity offers a good field for radical surgery as well as radical radiation and that the regional lymph nodes provide a helpful barrier in the delay of neoplastic extension distally.

The most consistent pattern of bone metastasis is that to neighboring portions of the skeleton from cancer of the prostate.

Epidermoid carcinoma, if metastatic to bone, almost always produces osteolytic metastases.

Search of sputum for metastatic tumor cells is desirable on the basis of x-ray and clinical signs of bronchial communication from secondary foci in lungs as well as from primary foci.

Myelography, angiography and genitourinary and gastrointestinal studies should be employed more frequently for the evaluation of possible soft-tissue metastatic foci in corresponding areas.

In my experience, x-ray recognition of cardiac and pericardial invasion lags behind the autopsy incidence sufficiently to emphasize the need for a more accurate evaluation of this question by other methods.

A tendency for symmetrical collapse of osteoporotic vertebras not involved with cancer and for asymmetrical collapse of those so involved is suggested as a helpful differential criterion.

Three criteria are suggested for selection and prognosis of patients treated by resection of metastatic foci.

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References

1. Kasdon, S. C., Fishman, W. H., Dart, R. M., Bonner, C. D., and Homburger, F. Methylandrostenediol in palliative treatment of breast cancer. *J. A. M. A.* **148**:1212-1216, 1952.
2. Freedberg, A. S., Ureles, A. L., Lesses, M. F., and Gargill, S. L. Pulmonary metastatic lesion successfully treated with radioactive iodine: report of case of pulmonary metastasis from papillary adenocarcinoma of thyroid. *J. A. M. A.* **144**:16-19, 1950.
3. Frantz, V. K., Larsen, W. G., and Jaretzki, A., III. Evaluation of radioactive iodine therapy in metastatic thyroid cancer. *J. Clin. Endocrinol.* **10**:1084-1091, 1950.
4. Sherman, A. J., Bonebrake, M., and Allen, W. M. Application of radioactive colloidal gold in treatment of pelvic cancer. *Am. J. Roentgenol.* **66**:624-638, 1951.
5. Roswit, B., and Kaplan, G. Nitrogen mustard as adjunct to radiation in management of bronchogenic cancer. *Radiology* **57**:384-394, 1951.
6. Freid, J. R., and Goldberg, H. Treatment of metastases from cancer of breast. *Am. J. Roentgenol.* **63**:312-326, 1950.
7. Paul, K. Die Behandlung der Knochenmetastasen der Brustkrebses mit Röntgenstrahlen. *Chirurg* **20**:367-370, 1949.
8. Moore, G. E., and Walker, W. W. Metastatic hypernephroma of thyroid gland with subsequent thyroidectomy, nephrectomy, and resection of pulmonary metastases. *Surgery* **27**:929-934, 1950.
9. Seiler, H. H., Clagett, O. T., and McDonald, J. R. Pulmonary resection for metastatic malignant lesions. *J. Thoracic Surg.* **19**:655-679, 1950.
10. Taylor, G. W. Surgical management of cervical lymph node metastases. *Radiology* **55**:60, 1950.
11. Zeidman, I., and Buss, J. M. Transpulmonary passage of tumor cell emboli. Presented at a meeting of the American Association of Pathologists and Bacteriologists, New York City, April 10, 1952.
12. Warren, S., and Gates, O. Fate of intravenously injected tumor cells. *Am. J. Cancer* **27**:485-492, 1936.
13. Aylwin, J. A. Avoidable vascular spread in resection for bronchial carcinoma. *Thorax* **6**:250-267, 1951.
14. Brandes, W. W., White, W. C., and Sutton, J. B. Accidental transplantation of cancer in operating room, with case report. *Surg., Gynec. & Obst.* **82**:212-214, 1946.
15. Martzloff, K. H., and Manlove, C. H. Vaginal and ovarian metastases from hypernephroma. *Surg., Gynec. & Obst.* **88**:145-154, 1949.
16. Cohen, A. G. Solitary pulmonary metastasis with detectable bronchial involvement appearing nine and a half years after resection of colon carcinoma. *New York State J. Med.* **50**:1848-1850, 1950.
17. Solomon, H. A., and Kreps, S. I. Twenty-six years of survival following carcinoma of sigmoid with prolonged liver metastasis. *J. A. M. A.* **144**:221-224, 1950.
18. Turner, J. W., and Jaffe, H. L. Metastatic neoplasms: clinical and roentgenological study of involvement of skeleton and lungs. *Am. J. Roentgenol.* **43**:479-492, 1940.
19. Willis, R. A. *The Spread of Tumors in the Human Body.* 550 pp. London: J. & A. Churchill, Ltd., 1934.
20. Abrams, H. L., Spiro, R., and Goldstein, N. Metastases in carcinoma: analysis of 1000 autopsied cases. *Cancer* **3**:74-85, 1950.
21. Abrams, H. L. Skeletal metastases in carcinoma. *Radiology* **55**:534-538, 1950.
22. Banyai, A. L. Metastatic tumors of lungs. *Dis. of Chest* **17**:681-690, 1950.
23. Warren, S., Harris, P. N., and Graves, R. C. Osseous metastasis of carcinoma of prostate with special reference to perineural lymphatics. *Arch. Path.* **22**:139-160, 1936.
24. Batson, O. V. Function of vertebral veins and their role in spread of metastases. *Ann. Surg.* **112**:138-149, 1940.
25. *Idem.* Role of vertebral veins in metastatic processes. *Ann. Int. Med.* **16**:38-45, 1942.
26. *Idem.* Vertebral vein system as mechanism for spread of metastases. *Am. J. Roentgenol.* **48**:715-718, 1942.
27. Brason, F. W., Eschner, E. G., Sanes, S., and Milkey, G. Secondary carcinoma of phalanges. *Radiology* **57**:864-867, 1951.

28. Sherman, R. S., and Ivker, M. Roentgen appearance of thyroid metastases in bone. *Am. J. Roentgenol.* **63**:196-203, 1950.
29. Escovitz, W., and White, S. G. Extensive metastatic calcification in case of malignant melanoma. *Ann. West. Med. & Surg.* **4**:339-342, 1950.
30. Nathanson, L. Calcified metastatic deposits in peritoneal cavity, liver and right lung field from papillary cystadenocarcinoma of ovary. *Am. J. Roentgenol.* **64**:467-469, 1950.
31. Turner, J. W. Diaphragmatic abnormalities secondary to tumors: roentgenologic study. *New Eng. J. Med.* **224**:936-940, 1941.
32. Ellis, F. H., Jr., Woolner, L. B., and Schmidt, H. W. Metastatic pulmonary malignancy: study of factors involved in exfoliation of malignant cells. *J. Thoracic Surg.* **20**:125-135, 1950.
33. Cross, G. O., and Pace, J. W. Malignant pheochromocytoma with paroxysmal hypertension and metastases to cervical spine. *J. A. M. A.* **142**:1068-1070, 1950.
34. Frank, H. A. Hypertrophic pulmonary osteoarthropathy simulating rheumatoid arthritis. *New Eng. J. Med.* **247**:283-285, 1952.
35. Robertson, C. K., and Russell, J. T. R. Bronchial cancer as cause of heart block. *Edinburgh M. J.* **57**:257-260, 1950.
36. Herbut, P. A., and Maisel, A. L. Secondary tumors of heart. *Arch. Path.* **34**:358-364, 1942.
37. Ritchie, G. Metastatic tumors of myocardium: review of 16 cases. *Am. J. Path.* **17**:483-489, 1941.
38. McCort, J. J., and Robbins, L. L. Roentgen diagnosis of intrathoracic lymph-node metastases in carcinoma of lung. *Radiology* **57**:339-360, 1951.
39. Dotter, C. T., Steinberg, I., and Holman, C. W. Lung cancer operability: angiocardiographic study of 53 consecutive proved cases of lung cancer. *Am. J. Roentgenol.* **64**:222-238, 1950.
40. Waddell, R. L. Anaplastic carcinoma of lung with metastases to spinal cord: case report. *Virginia M. Month.* **77**:77, 1950.
41. Hartman, H., and Helfer, L. M. Metastatic tumors involving central nervous system. *Texas State J. Med.* **37**:587-592, 1942.
42. Epstein, B. S. Myelographic diagnosis of epidural metastases in lumbosacral spinal canal. *Am. J. Roentgenol.* **68**:730-735, 1952.
43. King, A. B., and Ford, F. R. Clinical and anatomical study of neurological conditions resulting from metastases in central nervous system due to carcinoma of lung. *Bull. Johns Hopkins Hosp.* **70**: 124-156, 1942.
44. Hare, H. F., and Haggart, G. E. Osteitis condensans ilii. *J. A. M. A.* **128**:723-727, 1945.
45. Sweigert, C. F., Turner, J. W., and Gillespie, J. B. Clinical and roentgenologic aspects of coccidioidomycosis. *Am. J. M. Sc.* **212**:652-673, 1946.
46. Reyes, V., and Horrax, G. Metastatic melanoma of brain: report of case of unusually long survival period following surgical removal. *Ann. Surg.* **131**:237-242, 1950.

EVENTS LEADING TO MAJOR AMPUTATION IN PATIENTS WITH ARTERIOSCLEROSIS*

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THE treatment of arteriosclerosis of the legs has changed considerably in the past several years, notably through the introduction of antibiotics and anticoagulants and through the recognition of the value of sympathectomy. These advances have been accompanied by a substantial reduction in the incidence of major amputation. A further reduction in the loss of extremities might follow a clearer recognition of the causes of gangrene or of causes not formerly appreciated. Added benefit should result from scrutiny of treatment of the arteriosclerotic patient, and especially of methods of handling a necrosis that is still localized.

To obtain information bearing on these questions we have analyzed the clinical history and pathology of the limb in 73 patients, both diabetic and nondiabetic, on whom amputations were performed because of arteriosclerosis, at the Peter Bent Brigham Hospital, between 1945 and 1952. Ischemia was basic in all patients. No cases are included of amputation necessitated by either diabetic neuropathy or infection alone. Five cases of peripheral embolism occurring in arteriosclerotic arteries are included. Seventeen patients lost both legs; the study therefore comprises 90 extremities. In 6 patients (7 legs) a mid-leg amputation had been performed; in the remainder, the amputation was performed above the knee. The cases are consecutive except for the discarding of several in which the pathological data were incomplete. Cases of traumatic amputation are also excluded.

In analyzing these cases we have classified the responsibility for the loss of the leg as one of three types: spontaneous evolution of the arteriosclerosis and its complications, which we are unable to control by means currently at our disposal; injury, accidental or inflicted by the patient, or resulting from neglect by the patient; and faulty medical management.

TABLE 1. *General Data on Patients.*

GROUP	NO. OF PATIENTS	MALE PATIENTS	FEMALE PATIENTS	AGE		DOUBLE AMPUTATIONS*	POSTOPERATIVE DEATHS
				AVERAGE yr.	RANGE yr.	NO. OF CASES	
Diabetic patients	39	14	25	68	43-86	12(32%)	3(8%)
Nondiabetic patients	34	24	10	70	50-89	5(17%)	7(20%)
Totals	73	38	35			17(25%)	10 (14%)
Average				69	—		

*Percentages obtained by comparison with survivors of first amputation rather than total number of cases.

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Disease Leading to Amputation

Characteristics of the Patients

We may first inquire into the clinical profile of the patients. They may be characterized as patients of middle or old age, more often diabetic, as often women as men and, in the majority of cases, suffering from serious visceral impairment (Tables 1 and 2). The poor condition of the patients was reflected in the immediate postoperative mortality of 14 per cent (10 cases). Four of the deaths followed a second amputation.

Table 2. *Concomitant Condition before Terminal Disease of the Leg.*

Condition*	No. of Cases
Arteriosclerotic heart disease	22
Severe hypertension (with or without heart disease)	14
Cerebrovascular disease (including recent hemiplegia)	7
Postoperative state	3
Others (pulmonary tuberculosis, cancer, malnutrition)	4
Total	50

*Cerebrovascular disease included in other categories was present in 10 cases, and other conditions included in other categories in 12.

Diabetes existed in twice as many women as men. In the majority of the diabetic patients (28 out of 39) the disease was known to have been present for five to twenty-five years. In 24 patients the daily insulin requirement was 15 units or more. The increased susceptibility of the diabetic patient to infection (Table 3) was evidently responsible for the greater incidence of both single and double amputations in this group.

Local Problem

Most patients had been aware of difficulty in the leg for a relatively short time before the amputation became necessary (Table 4). It was therefore not a simple progression of the arteriosclerosis that most often led to amputation, but rather the occurrence of one of two complications — arterial thrombosis or infection (Table 3). The occasional role of venous thrombosis and of cutaneous infarction in precipitating gangrene has been noted in an earlier report.[1]

Table 3. *Pathologic Condition Initiating Deterioration of Leg.**

Condition	Diabetic Patients	Nondiabetic Patients	Totals
Arterial thrombosis	17	24	41
Infection	28	8	36
Venous thrombosis	1	3	4
Peripheral arterial embolism:			
From auricular fibrillation	2	1	3
From myocardial infarction	—	1	1
Aneurysm:			
Aortic, by embolism	—	1	1
Popliteal, by thrombosis	—	1	1
Cutaneous infarction	3	—	3
Totals	51	39	90

*Totals refer to 90 legs in 73 patients.

Table 3 shows that infection occurs more frequently in the diabetic than in the nondiabetic patient. This is consistent with the fact that gangrene often occurs in the diabetic patient with only moderately advanced arteriosclerosis. In the nondiabetic person, on the other hand, gangrene generally occurs because of obstruction of larger arteries by thrombosis, a fact emphasized in a previous publication.[2]

Table 4. *Duration of Symptoms (in Single, or First, Amputations).*

Duration	Diabetic Patients	Nondiabetic Patients	Totals
Less than 1 mo.	14	13	27
1 month to 1 yr.	13	12	25
1 to 5 yr.	6	5	11
5 to 10 yr.	5	2	7
More than 10 yr.	1	2	3

The treatment given is of interest. Antibiotics and anticoagulants were used frequently — perhaps, as pointed out below, insufficiently. Sympathectomy was done in 15 patients, but in all cases only after the terminal disease of the leg was well established. Causes for failure of the operation are given in Table 5. The operation made 2 limbs worse; these were probably already doomed. Embolectomy was attempted in 3 of the 4 patients with embolism of cardiac origin, but the operation failed because of extensive secondary thrombosis. Amputation of a toe in 24 cases and transmetatarsal amputation in 3 preceded the removal of the leg (Table 6). In all cases necrosis and infection supervened or continued.

Table 5. *Causes of Failure of Sympathectomy.**

Cause of Failure	No. of Cases
Postoperative venous thrombosis	2
Postoperative arterial thrombosis	3
Persistent sympathetic activity after extensive operation	2
Infection too far advanced	4
Ischemia irreversible	3
Ischemia increased after postoperative rupture of gastric ulcer	1

*All operations were done during the terminal disease of the leg; 6 patients were diabetic, and 9 nondiabetic.

Table 6. *Antecedent Local Operations.*

Operation	No. of Cases
Toe amputation	24
Transmetatarsal amputation	3
Incision and drainage of infection	3
Débridement of toe or foot	4
Guillotine amputation of leg or thigh (as planned procedure preliminary to thigh amputation)	6

Responsibility for Loss of Extremity

In attempting to explain the loss of the extremity, we have assumed that when the patient and the physician each exercised average care in the handling

of the disease, the responsibility must be attributed to the disease itself. Two thirds of the cases fell in this category. The remaining third could be divided into two almost equal groups: in one the patient himself seemed responsible, and in the other, medical care appeared at fault (Table 7). In a similar study of gangrene made by Barker[3] in 1935, the responsibility of the patients and physicians appeared even greater.

Table 7. *Summary of Events Leading to Amputation.*

Cause of Amputation		Diabetic Patients	Nondiabetic Patients	Totals
Spontaneous evolution of arteriosclerosis and its complications		30	30	60 (67%)
Injury, or neglect by patient:		15	2	17 (19%)
Poor hygiene and poor control of diabetes	5			
Failure to heed symptoms	1			
Self-treatment of infection	4			
By escharotic or irritating drugs ("Freezone," "Lysol," "Minit-Rub")	3			
By trimming nail	1			
Accidents:				
Contusion	2			
Burn	1			
Faulty medical management:		6	7	13 (14%)
Failure to recognize nature of disease	4			
Failure to treat infection properly	3			
Failure to anticipate or treat thrombosis of arteries or veins	3			
Poor technic of minor amputation or débridement	3			

Injury, or Neglect, by Patient

The attitude and actions of the patient were of great significance, especially among the diabetic patients. In this group particularly, local hygiene and poor diabetic control predisposed to infection. Diminution of sensation associated with neuritis often prevented the patient from realizing that the limb was being injured.

Case 1. A 68-year-old woman noted pain about the left great toenail. She trimmed the nail, injuring the nail bed slightly, but sought no medical advice for 2 months. By that time an ulcer had formed at the site of injury, and the entire nail plate was floating in pus. She was admitted to the hospital, where diabetes was discovered, requiring up to 30 units of insulin a day. The toe was gangrenous by this time. No pulses were present below either femoral level. The toe was amputated, and an abscess of the dorsum of the foot was drained. Three days later gangrene of the 2d toe had developed. A mid-thigh amputation was done. An incomplete thrombosis of the femoral artery was found at the level of section. This was presumably the distal end of a process completely occluding the artery at a higher level.

In this case it seems likely that the patient's attention was first attracted to the great toe because of ischemia early in the development of the arterial thrombosis.

Case 2. At the age of 72 diabetes was discovered in this man, requiring 10 units of insulin daily. At the age of 75 he burned the right leg by coming in contact with live steam. Infection and gangrene quickly followed, and a right mid-thigh amputation was done. At the age of 78 he stubbed the left 5th toe against a couch with sufficient violence to avulse the nail. An ulcer promptly developed, with cellulitis of the foot. After 6 weeks of treatment a left transmetatarsal amputation was done. Osteomyelitis was present in the 5th metatarsal head. Ten months later there was spontaneous necrosis of the metatarsal amputation scar, with extensive necrosis of the foot. Amputation was performed through the middle of the leg, with prompt healing.

Case 3. An obese, old-looking woman of 43 in whom diabetes had been discovered at the age of 31, had refused to follow a diet or to take insulin, the daily requirement of which was 15 to 30 units. She had suffered from pain in the legs and numbness in the toes for 5 years. For 2 years there had been a callus under the 2d metatarsal head, probably on the basis of the neuropathy. This had caused sepsis and osteomyelitis of the 2d metatarsal head and the proximal phalanx of the 2d toe. During this time she frequently walked about when a frank abscess had developed, refusing to stay off her feet. On 3 occasions an abscess had been drained.

Three weeks before admission cellulitis of the foot, with chills and fever, developed. No pulses were found below the right femoral or left popliteal levels. The patient was unco-operative and withdrawn mentally.

An amputation of the 2d toe and metatarsal head was done with a long incision on the sole of the foot to drain an abscess. Three minor débridements were necessary for small areas of necrosis of the wound edge. Split-thickness skin grafts were applied. After 3 months the wound was almost healed except for a small area proximally. Sympathectomy was advised to aid in the healing, but was refused. The patient was discharged home and followed in the outpatient department. Three weeks later the infection became active, and massive gangrene resulted. A guillotine amputation was done at the ankle, followed in a few days by an amputation through the middle of the leg.

Case 4. A 72-year-old man had diabetes discovered 10 years earlier. Treatment had been refused until 1 year before admission, when he agreed to take 15 units of N.P.H. insulin daily. The control of the diabetes was nevertheless erratic, with much fluctuation of urine sugar and with the frequent presence of acetone.

He neglected to keep his feet clean, and frequently had minor infections of his toes and feet. The exacerbation of one of these infections suddenly produced gangrene of the right 3d and 4th toes. These toes were amputated in a guillotine fashion. In spite of the drainage thus afforded and intensive antibiotic treatment, chills and fever developed, and on the afternoon of the next day a guillotine amputation was done through the upper tibial level. Eight days later an ordinary closed supracondylar right-thigh amputation was performed. Examination of the arteries showed moderate arteriosclerosis, with new thrombosis. Healing was good, and an artificial limb was fitted and worn.

A year and a half later the patient put his left foot into water that was apparently too hot, for it blistered the sole of the foot. There was some evidence of neuritis with diminution of sensation. The diabetes had again gone out of control, with much sugar in the urine. The foot was dressed, and it healed. Ten months later blisters developed on the sole of the left foot as a result of chafing in a loose shoe. Two days later the blisters became infected; chills and fever occurred. He entered the hospital where the sole was débrided, a healthy-appearing base being obtained. A few days later a split-thickness skin graft was applied, but this sloughed, and there was further infection. A definitive amputation was then done through the middle of the

left leg. At operation both the anterior and posterior tibial arteries showed a spurting flow.

CASE 5. A hypertensive, 66-year-old woman with diabetes suffered a blister of the left heel, which she treated at home for 2 months with Lysol soaks. At the end of this time the heel was deeply necrotic and black. A left supracondylar amputation was done. The arteries showed arteriosclerosis, with no thrombosis.

Faulty Medical Management

In 4 cases the treatment was at fault, owing to failure to recognize the true nature of the disease.

CASE 6. A 68-year-old woman, suffering from arteriosclerotic heart disease, had a painful corn over the left 5th toe. The corn was removed in a doctor's office, in spite of the fact that no pulse was present below either femoral level. Infection followed this procedure, and the foot became progressively more painful and swollen. At the end of 3 1/2 months a small abscess was present beneath the site of the corn. The toe was amputated, and the wound sutured. Examination of the amputated specimen showed osteomyelitis of the proximal phalanx. Postoperatively the wound broke down, with increased infection and fever. A low-thigh amputation was done. The amputated limb showed arteriosclerosis without thrombosis.

In this case both the excision of the corn and the immediate suture of an amputation close to a septic area seems to have been inadvisable.

CASE 7. A 79-year-old woman had had diabetes for 6 years, requiring up to 45 units of insulin daily. Arteriosclerotic heart disease and hypertension were also present. Four weeks before admission to the hospital, a spontaneous ulcer, 1 cm. in diameter, developed in the midlateral portion of the right leg. This was apparently a spontaneous skin infarction. A feeble dorsalis-pedis pulse was present, but no posterior tibial pulse. Because the ulcer was sluggish in healing, a few small varices present in the leg attracted the attention of the surgeon, who performed multiple ligations of the right saphenous vein, with 3 incisions in the leg proper. An incision close to the ulcer broke down and became confluent with the original ulcer. This was grafted with a split-thickness graft, but the edges became necrotic, and a low-thigh amputation became necessary. Examination of the limb showed thrombosis of the peroneal artery and narrowing of the popliteal and anterior tibial vessels.

CASE 8. A 79-year-old man complained of progressively increasing pain of the right midcalf and foot during treatment for arteriosclerotic heart disease. No active treatment was undertaken for the limb, despite the recognition of the presence of a small popliteal aneurysm. On the 7th hospital day the pulses of the right foot and the popliteal pulse, which had been present on admission, disappeared. The limb became gangrenous, and a right supracondylar amputation was done. A thrombosed popliteal aneurysm was found. The early symptoms had apparently been caused by emboli from parietal thrombosis in the aneurysm.

In 6 patients treatment of infection or thrombosis was inadequate:

CASE 9. A 67-year-old man had had arteriosclerotic heart disease for 10 years. He injured the right great toe in cutting the nail. A mild cellulitis resulted, for which he was treated as an outpatient for 4 weeks. No pulses were present below the femoral level. Because of the apparent mildness of the infection, no antibiotics were given. At the end of 4 weeks the great toe suddenly turned black. A left low-thigh amputation was necessary.

CASE 10. A 65-year-old woman entered the hospital with a history of sudden pain and tingling of the right lower extremity. Physical examination showed a slightly enlarged heart, with basal rales. There was serious ischemia to midthigh level. There was obvious thrombosis of the superficial venules of the limb, and no pulse even at the iliac level. She was given heparin in the hope that this would prevent further thrombosis and that the obviously necessary amputation might be performed at a lower level. Five days later a right high-thigh amputation was performed. In spite of the fact that a diagnosis of thrombosis of the right common iliac artery was made, no anticoagulants were given after the amputation. On the 5th postoperative day a thrombosis of the left superficial femoral artery developed. She died on the day after this 2d thrombosis. Autopsy revealed that the cause of death was arteriosclerotic heart disease with terminal aspiration pneumonia. The thrombosis involved the left superficial femoral artery and the popliteal artery, which showed a small aneurysm. There was thrombosis of the peroneal and anterior tibial veins, seemingly of an agglutinative type.

Poor technic in surgical procedures on the foot appeared responsible for the loss of the limb in 3 cases. This included too wide a dissection and immediate closure of toe amputations performed for sepsis and, in 1 case, a wide, u-shaped débridement in the foot.

CASE 11. A 65-year-old woman had claudication of 7 months' duration. One month before admission a thrombosis of the popliteal artery developed. Because the foot became painful she consulted a chiropodist, who "lanced" the right heel, as well as an infection in the space between the 1st and 2d toes. In the next 2 weeks infection became more evident at both sites. On admission there was an infection at the base of the 2d toe. Amputation of this toe was done, with a wide u-shaped débridement of the tissues at its base, including the metatarsal head. In the next few days the great toe became gangrenous, and a supracondylar amputation was necessary.

DISCUSSION

It is apparent that the present low rate of amputation can be reduced still farther if the information already available is applied more carefully.

It is unfortunate that all patients with arteriosclerosis do not have a history long enough to give a warning of impending trouble, but some at least do. Since in this hospital we care for ischemic limbs in at least four times as many nondiabetic as diabetic patients, the relatively large number of the latter who require amputation indicates the greater risk for the diabetic patient. Moreover, diabetes apparently favors the development of arteriosclerosis in women (Table 1). Physicians should do a better job of teaching local hygiene in all arteriosclerotic patients. Infection is the complication responsible for about a third of all amputations. Cleansing, with soap and water, the prophylaxis and treatment of dermatophytosis by a bland material, such as Desenex powder, the avoidance of corn cures and other harsh chemicals, including allergenic solutions and salves, such as penicillin ointment, and the wearing of soft, heavy socks in well fitting shoes are all important. Really careful control of diabetes is, of course, vital. Once infection has developed, meticulous attention is necessary in the proper choice and dosage of the antibiotics.

The arteriosclerotic or diabetic patient must never be dismissed from attention. At periodic examinations the doctor should determine whether or not the arteriosclerosis is progressing, and whether the patient is following a proper regimen.

The physician has other obligations when seeing the patient in the chronic stages of the disease. In our experience sympathectomy done in the chronic stages of arteriosclerosis affords substantial protection against future loss of the extremity. Sugges-

tions for wider application of this operation were made in a previous report.[4] Sympathectomy is especially called for on the side of the surviving leg after amputation, since the incidence of later amputations is as high as 40 per cent.[5, 6] It is preferable to perform the sympathectomy before the patient leaves the hospital after an amputation. From data in the earlier report,[4] as well as the present one, it is apparent that sympathectomy should not be done in an effort to halt advancing infection or gangrene. Moreover, it cannot be counted on to lower the level of a necessary amputation. Nevertheless, once the condition of the limb is stabilized, sympathectomy often proves extremely valuable, particularly for localized necroses. The use of heparin should at least be considered in every case after sympathectomy, to prevent postoperative venous or arterial thrombosis.

Occasionally, a leg is lost (2 cases in the present series) from an episode of infection in a chronic varicose ulcer or dermatitis in an arteriosclerotic limb.[7] Adequate treatment of such lesions should prevent some amputations. A toe showing a chronic crust or sinus almost invariably harbors osteomyelitis or joint sepsis, despite negative x-ray findings. The infection may suddenly become apparent without warning, threatening the extremity. Planned amputation of such toes should therefore be done on clinical grounds.

We do not have as yet sufficient data to know whether aortic or peripheral aneurysms should be treated if they are not symptomatic, but the incidence of loss of the limb, once a popliteal aneurysm has given rise to symptoms, is so high as to make it imperative that such lesions be corrected.[8] Early symptoms caused by small emboli from a parietal thrombus often precede complete occlusion.

Patients with arteriosclerosis or diabetes cannot withstand infections that would be trivial in other persons. Bed rest, simple wet dressings of saline or boric acid solution and early and adequate constitutional antibiotic therapy are essential. Here, as in other conditions requiring bed rest, the heel should be protected from pressure, but with the head of the bed elevated to place the heart above toe level.

The diagnosis of arterial thrombosis will be made more frequently if the great incidence of this complication is kept in mind. The symptoms are those of acute arterial obstruction, closely resembling arterial embolism. The same clinical conditions that precipitate venous thrombosis (myocardial infarction, heart failure, hemiplegia and surgical operation) often precipitate arterial thrombosis. Thrombosis in either an artery or a vein is often followed by further thrombosis. Heparin, in our experience, is the drug of choice for these complications. We believe that 2 extremities in this series were lost through venous thrombosis on sudden withdrawal of heparin, and therefore advise a gradual termination of a course of heparin treatment.

The lodgment of an embolus in an arteriosclerotic artery gives a much worse prognosis than one in a normal vessel. This is due to early and extensive propagation of thrombus and greater technical difficulties in performing an embolectomy. The rule to perform an indicated embolectomy early is particularly important in arteriosclerosis.

Cutaneous infarction should be recognized as a distinct entity in the course of arteriosclerosis.[1] It represents localized ischemia, often out of proportion to the vascularity of the remainder of the leg. Prompt excision, with skin grafting and sympathectomy, all at one sitting, appears to be the treatment of choice. The common "cracks" of the heel should be recognized as small spots of necrosis.

The success of toe amputation is of tremendous importance to the patient. The procedure should be carried out with the utmost gentleness and care. A transmetatarsal amputation often affords a better chance of healing than a toe amputation. Furthermore it removes the hazard of later necrosis of remaining toes. The incision should be circular, although in a toe amputation a racket incision with a short longitudinal cut may allow the bone to be divided with least manipulation. No undercutting should be done; the skin must not be grasped with any instrument; the periosteum should not be retracted; and any tissue inadvertently crushed by instruments should be excised. Deep ligatures and sutures should be avoided, fine, plain catgut being used when essential. Finally, the wound should be left open if the amputation is done while acute or subacute infection is still present.

Incisions for drainage should be made in the long axis of the part. Débridement of the toes or foot is sometimes successful but, if wide, may give rise to necrosis of neighboring parts. This is not to gainsay the value of an open guillotine amputation in infection. Débridement of the heel or leg offers a better chance of success, especially if a skin graft is applied immediately.

Several other warnings seem necessary. An accurate appraisal of the state of the peripheral arteries should be part of every examination. The elderly person with sudden occurrence of pain in a toe is usually suffering from arterial thrombosis. Avulsion of a nail, or an operation for ingrown toenail in such a person, almost invariably produces gangrene. Incisions below the knee are extremely dangerous in patients with deficient blood supply. Likewise, manipulation of a joint, the use of diathermy, and the application of casts have occasionally produced gangrene and demand great caution.

Summary and Conclusions

The majority of extremities requiring amputation in arteriosclerotic and diabetic patients are lost through arterial thrombosis or infection. In a smaller number, gangrene is occasioned by venous

thrombosis, peripheral arterial embolism, aneurysm or cutaneous infarction.

In the present study of 90 major amputations in 73 patients, injury, neglect by the patient and faulty medical management were probably responsible for a third of the amputations.

A reduction in the number of extremities lost is possible. An accurate appraisal of the peripheral arteries should become part of every general examination. The doctor must exert even more effort to teach the patient proper hygiene and control of diabetes. Sympathectomy and other measures to increase blood supply should be more widely applied in the chronic stages of arteriosclerosis. Finally, the doctor must remain alert to the signs of complications that cause gangrene and treat them more vigorously when they occur.

References

1. Edwards, E. A. Atypical manifestations of peripheral arteriosclerosis. *New Eng. J. Med.* **247**:627-631, 1952.
2. *Idem. Thrombosis in Arteriosclerosis of the Lower Extremities.* (American Lecture Series.) 74 pp. Springfield, Illinois: Charles C Thomas, 1950.
3. Barker, N. W. Danger of gangrene of toes in thrombo-angiitis ob iterans and arteriosclerosis obiterans. *J. A. M. A.* **104**:2147-2149, 1935.
4. Edwards, E. A., and Crane, C. Lumbar sympathectomy for arteriosclerosis of lower extremities. *New Eng. J. Med.* **244**:199-204, 1951.
5. Silbert, S. Mid-leg amputations for gangrene in diabetic. *Ann. Surg.* **127**:503-512, 1948.
6. McKittrick, L. S. Diabetic gangrene: review of nine hundred and seventy-two cases of gangrene associated with diabetes mellitus treated at New England Deaconess Hospital. *Arch. Surg.* **40**: 352-363, 1940.
7. Edwards, E. A. Necrotic lesions of leg in arteriosclerosis. *New Eng. J. Med.* **239**:571-575, 1948.
8. Gifford, R. W., Hines, E. A., and Janes, J. M. Analysis and follow-up study of 100 popliteal aneurysms. *Surgery* **33**:284-293, 1953.

THE IMPORTANCE OF THE PSYCHOLOGIC FACTOR IN GYNECOLOGY*

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KNOWLEDGE of the sexual and reproductive functions of women has been built into the specialty of gynecology with contributions not only from obstetricians and surgeons, from endocrinologists and physiologists, but also from the field of psychiatry, in which one may learn the psychologic meaning of sex to a person and her reactions and attitudes to her role as a woman and mother.[1-11]

Every general practitioner no doubt encounters almost daily examples of the emotional element that often accompanies the normal changes in a woman's reproductive physiology. There is the general emotional upheaval at the menarche, the premenstrual depressions and tensions, the frustration caused by dyspareunia and frigidity, the unhappiness of some who are not pregnant and others who complain that they are, and the instability of the menopause. These are common, everyday experiences. In the specialty of gynecology more puzzling problems are frequently encountered. There may appear to be a close correlation between the emotional and endocrine systems. It is not always easy to demonstrate whether such apparent correlations are merely a strange series of coincidences or in fact examples of an emotional cause and its physical effect. I should like to mention briefly a few cases recently observed in the gynecologic clinic of the Peter Bent Brigham Hospital to illustrate the questions raised by some of these problems.

A young woman complaining of severe, incapacitating dysmenorrhea showed completely negative findings in extensive organic and endocrine investigation. Why should an apparently normal physiologic process as menstruation be accompanied by so much pain?

A young married woman complained of sterility. Extensive examination of her and of her husband, all modern technics being utilized, revealed no abnormal findings. Why was conception impossible for her? After she gave up all hope and adopted a child she became pregnant within a few months. What had changed in her endocrine and reproductive system? Where and how did these changes occur?

A young unmarried woman who was afraid of pregnancy after sexual exposure missed her next period by over three weeks. When learning that a pregnancy test was negative, she started to menstruate a few days later. What had happened to her previously normal menstrual cycle? And how was this change effected?

A twenty-year-old girl presented herself with a history of never having menstruated. There were no abnormalities on physical examination; she had a normal basal metabolic rate, normal urinary 17 ketosteroids and normal follicle-stimulating hormone, but she did not ovulate. The diagnosis was "hypothalamic amenorrhea."[12] What inhibited the normal pituitary-ovarian functioning and the establishment of a normal menstrual cycle?

A thirty-one-year-old married woman presented herself with a history of amenorrhea of three months duration, constipation, morning sickness and marked weight gain. Ever since her menarche at the age of sixteen she had had long periods of amenorrhea. She had also felt increasingly distressed over her failure to conceive over the five years of her married life. Physical examination revealed breast changes char-

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acteristic of pregnancy, a softened cervix and a slightly enlarged uterus. A pregnancy test was positive. The patient, feeling very happy, was referred to an obstetrician; however, because her uterus did not enlarge adequately, an x-ray examination was made at the fifth month. It showed complete absence of fetal growth. The patient was informed of this and returned, very discouraged, to the clinic. A second pregnancy test was negative, and a biopsy showed endometrium in the proliferative stage. The breast changes receded. How could a strong fantasy of pregnancy in a woman cause hormonal changes sufficient to induce a positive pregnancy reaction in test animals?

Such cases have stimulated a study of how, if at all, emotions and attitudes of female patients may contribute to the symptomatology of gynecologic disease. Since the whole problem is a complicated one it was decided to start with a study of the menstrual disorders seen in the clinic — amenorrhea, oligomenorrhea and dysmenorrhea.

Since the investigation started as recently as eight months ago, this report can only indicate some of the questions that arise, methods being used and the assumptions that some of the findings suggest.

Patients with Dysmenorrhea

Each patient is first seen by the gynecologist; a thorough history, including a detailed menstrual chart, is taken, and a complete physical examination is performed. Premenstrual pregnanediol determinations are done to establish the occurrence of ovulation. Some of the patients receive estrogen therapy to suppress ovulation during one cycle and to give them the experience of a pain-free, estrogen-withdrawal flow.[13, 14] After this, the patient is referred to the psychiatrist for weekly psychiatric interviews, which serve a dual purpose: psychiatric research and psychiatric treatment. The psychologist gives the patient projective tests to help in a further understanding of some of the deeper underlying patterns that might not emerge in the interviews for some time. If the patient is an adolescent the mother is taken concurrently into observation and treatment by the psychiatric social worker. Throughout the period of observations and treatment, the patient is instructed to keep a detailed calendar of her menstrual periods (date, amount, flow, intensity and duration of pain and other symptoms), and to bring in weekly twelve-hour specimens for pregnanediol determinations during the latter half of the menstrual cycle.

The following case is typical.

A 14-year-old girl was referred because of severe, incapacitating dysmenorrhea. She had started to menstruate at the age of 12½ years. Her periods at first occurred at 2-week intervals and were asymptomatic; then the interval lengthened to 4 weeks. The periods at first were pain free, but at 13 she began to experience excruciatingly severe cramps accompanied by nausea and vomiting, which made it necessary for her to stay in bed for at least 2 days. About 2 weeks before admission she began to daydream in school, and her schoolwork, previously adequate, began to deteriorate. She had always been quiet, friendly and very conscientious. Being the oldest girl in a family of 6, she had taken on without overt protest an unusually large proportion of household duties.

Physical examination was negative, but the gynecologist noted that she was tense during the rectal examination. With a great deal of encouragement on the part of the psychiatrist, a good relation was eventually established, and although she found talking difficult she gradually told about the great discomfort of her dysmenorrhea, how she would like to be rid of the "whole thing," meaning the menses, and how she felt that there was "something wrong inside her" that produced the pain. She complained of her many duties at home and expressed resentment against her siblings, who "get away without doing housework" — the boys because they were boys, and the girls because they were younger. As soon as a relation of trust had been established with the psychiatrist 2 major changes were observed: the patient's dysmenorrhea disappeared, her periods at first reverting to the 2-week interval and then back to the 4-week interval, repeating the earlier pattern of her menarche (urine specimens assayed for pregnanediol showed that ovulation was occurring regularly); and the previously good girl became a behavior problem at home — she started to refuse to do some of the household tasks and became "saucy" when reprimanded by her mother or father. Concurrently, she overcame her learning difficulty at school.

After about 6 months of weekly psychiatric interviews she began to take more interest in her appearance. She also became interested in a boy, who started to call her for dates. This threw her into a conflict with her strict and old-fashioned parents and brought on fears in herself of being bad. She oscillated between her wish to go out on dates with the boy and her desire to be obedient to her parents and excel at school. With the appearance of this conflict, her previous symptom of dysmenorrhea has returned, and although she still ovulates, some of her periods have been 1 or 2 weeks late. At present, efforts are being made to help the patient understand this phase of her conflict.

This patient illustrates several points, which have been observed to a greater or lesser degree in most of the dysmenorrheic patients who considered their dysmenorrhea severe enough to warrant the seeking of medical aid:

The patient showed a conflict over growing up that expressed itself in the following ways: between her periods she was unusually willing to accept the responsibilities of an adult in her home; however, during her periods she stayed in bed with pain, expecting her mother to do every little thing for her — that is, she became a completely dependent child. In her interviews she expressed envy of her sisters, who were younger and were spared from household responsibilities. "It's no fun to be grown up." The normal adolescent conflict between the wish to be grown up and the wish to remain a child is magnified in the dysmenorrheic patient. The two sides of this are expressed in the behavior during the phases of each menstrual cycle. Between the periods of actual bleeding there is a striving for independence and taking on of adult activities to an unusually large degree. During the period there is a return to a particularly dependent and childlike behavior. At this time the patient expects the mother, husband or whoever is the closest person in the environment to fulfill her every need. This description is equally applicable to the older dysmenorrheic women. It is interesting that during the time of relief from menstrual

cramps and symptoms, the patient described above rebelled openly against her excessive household duties. The dysmenorrhea reappeared together with the appearance of a boy friend on her horizon, a boy she felt attracted to and was, therefore, very much afraid of. A similar configuration has been detected in some of the other patients.

In most of the patients, in addition to the physical symptoms of dysmenorrhea, at least one symptom indicative of a purely emotional difficulty has been observed. The patient described above, in spite of her normal intelligence, experienced learning difficulties at school that seemed to be connected with her fear of people in authority. Some patients experience more than usual difficulties in their social relations with people such as parents, siblings and friends; others find themselves hampered in their ability to perform to their full capacity in work, school or at home.

As in the case presented above, with the onset of psychiatric treatment an alteration of some kind in the whole menstrual pattern frequently occurred. This consisted of irregularities in the menstrual cycle and changes in the amount or duration of flow. These shifts occurred either in conjunction with the change in the intensity or character of the dysmenorrhea or independently of it. So far the appearance of anovulatory cycles has not been observed.

With the improvement of the dysmenorrhea under psychiatric treatment some actual disturbance of behavior often appeared at least temporarily. In the case discussed above, it was rebelliousness and aggressiveness at home. Another patient began to steal temporarily. Still another became somewhat promiscuous. This is interpreted as an indication that the dysmenorrhea expresses some emotional conflict that comes to the fore more directly when the physical symptom is relieved. It should be emphasized that the behavioral symptoms are again dealt with on a psychiatric level and tend to disappear as soon as further insight and understanding is gained by the patient.

Oligomenorrheic and Amenorrheic Patients

Before going into questions of a more general nature I should like to turn now to the oligomenorrheic and amenorrheic patients and again to introduce the subject with a description of a representative case.

Mrs. Y., a 25-year-old woman, had been married for 5 years. Her menarche had started at the age of 13, but her periods had been irregular from the onset. They occurred at intervals of 4 to 12 months. She was married at the age of 20, and 2 months later became pregnant. She miscarried in the 10th week of her pregnancy. Shortly afterward there was a 3-month period of amenorrhea diagnosed as possible pregnancy; however, it ended with a normal period. No products of conception were passed. Since then the patient has been under the constant study and care of a gynecologist. She was found to be normal on physical examination and had a normal basal metabolic rate, normal 17 ketosteroids excretion and normal excretion of follicle-stimulating hormone. Bleeding was occasionally induced by various endocrine treatments. During more than 2 years of gynecologic therapy there was only one episode of apparently spontaneous ovulation, which followed 3 months of amenorrhea and terminated in a so-called normal period. In September, 1952, all endocrine therapy was stopped, and the patient was referred to the psychiatric research unit. She was instructed to keep a calendar and to bring in weekly 12-hour urine specimens to determine ovulation. After a relation of trust had been established she stated that she wanted neither to menstruate nor to become pregnant. She had sought medical aid only at the insistence of her husband and mother, to prove to them that she was willing to co-operate. She admitted to a fear that there was something wrong with her "inside organs," and said that she would like to know what it was. (This woman is an intelligent college graduate who has been working ever since her marriage in a position that is socially higher than her husband's; she is very proud of her work and independent income.) She stated that she had wanted to be a boy; she had excelled in sports as a youngster and had later shifted her interest mainly to academic achievements. She was never interested in things feminine, in contrast to her older sister, who was "crazy about babies" and whom she considered "feminine and dumb." Her father had wanted a boy and was very disappointed when she turned out to be "just another girl." She stated that she had not wanted a child after her marriage but had not used any contraceptives because she thought she could not become pregnant. When she found out about her pregnancy she was disappointed and had a wish to get rid of the child. Although she did not actively interfere with the pregnancy she did not follow the doctor's instructions and, in fact, did the things he told her not to do. She was glad when she started to bleed and had the pains that accompanied the miscarriage. After the abortion she became afraid that she had caused some irreparable damage to herself and also regretted somewhat the loss of the child.

During this phase of her treatment she never ovulated but showed occasional staining. A turning point came when she gradually became aware of a deep but submerged wish to have a baby, in conflict with her desire to enjoy her freedom and to do as she pleased. She then asked her psychiatrist, a woman, if she had children of her own. When told "yes," she was surprised, looked happy and asked how it was possible to combine having children and a career. At about the same time the patient's sister became pregnant; this filled the patient with envy and an increasing desire to become a mother herself. She then remembered a period in her childhood when she had been filled with a wish to have a baby of her own.

During this phase the patient ovulated spontaneously and had a normal menstrual period. Four weeks without any evidence of ovulation or bleeding followed. Then she ovulated spontaneously and became pregnant, as evidenced by increasing pregnanediol titers, a positive pregnancy test and a physical examination performed by an obstetrician. She has now been pregnant for 18 weeks without showing any pathologic symptoms. Although she has continued to express fears and doubts about the pregnancy in her continued psychiatric treatment, she has been able to follow the instructions of her obstetrician and to accept increasingly her new responsibilities as an expectant mother.

This case, again, illustrates some of the points observed in the 5 cases of oligomenorrhea or amenorrhea now being studied. Like Mrs. Y., 3 patients of this group had the wish not to menstruate, either because they regarded menstruation as something ugly, sexual and thus forbidden or because they saw it as an indication of femaleness, which they rejected. They ostensibly came for treatment only because somebody in their family made them, and 2 of them refused treatment of any sort after a while.

Knowledge of these negative feelings about menstruation had not been obtained by the gynecologists. There are several reasons for this. The busy clinic atmosphere rarely lends itself to the develop-

ment of a sufficiently close relation for the patient to express such intimate feelings, and it takes some time to elicit them. Moreover, if a patient comes to a physician for treatment of a condition it is generally taken for granted that she genuinely desires improvement of that condition and, therefore, she is often not questioned about motivation.

Such apparently peculiar behavior on the part of these patients can be better understood if one looks more closely at Mrs. Y. She was conscious only of a desire *not* to menstruate and *not* to become pregnant. However, in the act of seeking medical aid she expressed her deeper and more basic wish to be a normal woman and mother, a wish that was in direct opposition to her conscious feelings, and became apparent to her only after prolonged psychiatric treatment.

All 5 patients with amenorrhea and oligomenorrhea so far seen have consciously rejected their role as women.

Discussion

Each patient with a menstrual disturbance thus far studied in the Gynecological-Psychiatric Unit has shown a definite emotional conflict. In the women with dysmenorrhea the predominant conflict seems to lie in the sphere of accepting adult feminine responsibilities. It is often expressed in excessive drive toward independence and activity between periods and giving in to childish, dependent wishes during the menstrual period. In the woman with functional amenorrhea and oligomenorrhea the sexual and reproductive roles of a woman's life are consciously unacceptable. The idea of femininity is rejected in favor of masculine behavior, or the idea of sex is associated with the sordid and the forbidden. At the same time these patients have a deep wish to be normal women and mothers that does not reach their conscious awareness for various reasons. These two psychologic configurations are not sharply delineated, but may merge into each other, as with the occasional patient with dysmenorrhea who has some menstrual irregularity or the patients with oligomenorrhea who have painful periods. The role of psychotherapy in such cases is to make the patients aware of their partly unconscious drives, to bring the inner conflict into the open, and to help them to arrive at a more satisfactory solution. If the conflict emerges into consciousness during psychotherapy, the gynecologic symptom often disappears. Temporary disturbances in behavior may then arise — that is, the patient expresses on a social level what she previously expressed in a bodily symptom. In such cases further psychiatric treatment is required. The constant correlation between emotional conflict and gynecologic symptoms has been apparent in this study of patients with various menstrual disorders. The added phenomenon of amelioration or disappearance of the symptoms with resolution of the conflict strongly suggests that emotional factors play an etiologic role in the production of certain menstrual dysfunctions.

In conclusion, I should like to say that these studies thus far indicate that the psychologic factor is important in gynecology. The difficult and important task for further research is to determine how, where and to what extent emotions and attitudes influence the delicate physiologic balance necessary for normal functioning of the female sexual and reproductive system.

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References

1. Abraham, K. Manifestations of female castration complex. In *Selected Papers*. 527 pp. London: Hogarth, 1929.
2. Benedek, T., and Rubenstein, B. B. Sexual cycle in women: relation between ovarian function and psychodynamic processes. In *Psychosomatic Medicine Monograph Series*. Vol. 3. 307 pp. Washington, D. C.: National Research Council, 1942.
3. Deutsch, H. *Psychology of Women*. Vol. 1. 480 pp. Vol. 2. 439 pp. New York: Grune & Stratton, 1944 and 1945.
4. *Idem*. Psychiatric component in gynecology. In *Progress in Gynecology*. Edited by J. V. Meigs and S. H. Sturgis. Vol. 2. 821 pp. New York: Grune & Stratton, 1950. Pp. 207-217.
5. Dunbar, H. F. *Emotions and Bodily Changes*. Second edition. 641 pp. New York: Columbia University Press, 1938.
6. Freud, S. Female sexuality. In *Collected Papers*. Edited by J. Strachey. Vol. 5. 396 pp. London: Hogarth, 1950. Pp. 252-272.
7. *Idem*. Some psychological consequences of anatomical distinction between sexes. In *Collected Papers*. Edited by J. Strachey. Vol. 5. 396 pp. London: Hogarth, 1950. Pp. 126-197.
8. Jones, E. Early female sexuality. *Internat. J. Psycho-Analysis* **16**: 263-273, 1935.
9. *Idem*. Early development of female sexuality. *Internat. J. Psycho-Analysis* **8**:468-472, 1927.
10. Lampl de Groot, J. Problems of femininity. *Psychoanalyt. Quart.* **2**: 489-518, 1933.
11. Wittkower, E., and Wilson, A. T. M. Dysmenorrhea and sterility: personality studies. *Brit. M. J.* **2**:586-590, 1950.
12. Sturgis, S. H. Amenorrhea: classification and treatment. In *Progress in Gynecology*. Edited by J. V. Meigs and S. H. Sturgis. Vol. 2. 821 pp. New York: Grune & Stratton, 1950. Pp. 163-175.
13. Sturgis, S. H., and Albright, F. Mechanism of estrin therapy in relief of dysmenorrhea. *Endocrinology* **26**:68-72, 1940.
14. Sturgis, S. H., and Meigs, J. V. Use of estradiol diproprionate in treatment of essential dysmenorrhea. *Surg., Gynec. & Obst.* **75**: 87-92, 1942.

MEDICAL PROGRESS

MYCOLOGY

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THE last Medical Progress report on mycology was presented in 1945 by Downing and Conant.[1] The present report covers the major advances in medical mycology since that time, and previous articles are used only for orientation. There have been tremendous advances in the field of medical mycology in the last eight years. A few of the milestones may be enumerated: the recognition of the benign, common forms of histoplasmosis; the diagnosis and surgical treatment of coccidioidal pulmonary residua; the treatment of blastomycosis with stilbenes; the utilization of periodic acid Schiff stain to demonstrate fungi in tissue; and the advance and utilization of immunologic procedures in mycology.

The field of medical mycology is small, and may be outlined as follows:

Systemic mycoses. Fungous infections of the various internal organs and systems are found in this group, and include coccidioidomycosis, histoplasmosis, blastomycosis, cryptococcosis, actinomycosis, nocardiosis, South American blastomycosis, mucormycosis, aspergillosis and geotrichosis.

Intermediate mycoses. These fungous infections are usually confined to the skin, mucous membranes, and subcutaneous tissue, but may become systemic. Best examples are moniliasis and sporotrichosis. For completeness, maduromycosis and chromoblastomycosis should be included here, and, in addition, rhinosporidiosis and some cases of *Trichophyton rubrum* infections may belong in this group.

Superficial mycoses (*dermatophytoses*). These are superficial fungous infections of hair, skin and nails. Clinically, this group is referred to as tinea capitis, tinea pedis, tinea corporis and so forth, depending on the location of the infection.

The subject is discussed under the two broad headings of clinical and laboratory mycology.

CLINICAL MYCOLOGY

SYSTEMIC MYCOSES

Coccidioidomycosis

This disease is present in two clinical forms: the common, primary, pulmonary type; and the rare, progressive, disseminated type. Sixty per cent of the cases of primary coccidioidomycosis are asymptomatic, and diagnosis is based chiefly on a positive coccidioidin skin test. The other 40 per cent are manifested by various nonspecific signs and symptoms of pulmonary infection.[2]

After the primary pulmonary infection, there are two important questions to be answered. The first is whether the progressive, disseminated form, with a 50 per cent mortality rate, will develop. The second is, if pulmonary residua appear, how are these lesions to be diagnosed?

Disseminated coccidioidomycosis. There are a number of criteria to determine whether dissemination will occur.

Duration of infection. If dissemination occurs, it is frequently within weeks and infrequently after a period of months. It rarely occurs in the second year.[2, 3] This appears to be a sound clinical observation, regardless of some dissenting opinion.[4, 5]

Sex. Dissemination is more common in the male.

Presence of erythema nodosum. This signifies a good prognosis[6] and further stresses the sex incidence, since it occurs in about 5 per cent of males and up to 35 per cent of females.[2]

Race. Nowhere in medicine is the racial predilection for a disease more strikingly demonstrated. Dissemination occurs in about 1 case out of 500 in Caucasian patients. The Mexican rate of the progressive disease is three and a half times that of the other Caucasian groups; the rate in Negroes is fourteen times, and the Filipino rate one hundred and eighty times[7] higher than that in whites. (Of interest is the fact that erythema nodosum is rare in Negroes.[6])

Reaction to coccidioidin. If the positive skin test reverts to negative, dissemination is imminent.[2]

Complement-fixation titer. The titer is low (1:2 to 1:16) in uncomplicated pulmonary disease. With dissemination, it may be found positive in dilutions above 1:16, with a tendency to rise. Thus, with a high complement-fixation titer and a negative skin test, prognosis is unfavorable.[2]

Presence of residual pulmonary cavities. With questionable exception, no case with residual pulmonary cavity has been known to disseminate.[3, 8] It is of interest that in a review of 53 cases of coccidioidal meningitis, 50 of which were fatal, Buss et al.[9] found that in no case in which there was pulmonary-cavity formation did coccidioidomycosis of the meninges develop.

Pregnancy. The incidence of dissemination in pregnancy is considerably greater than that reported in all cases of the disease, reaching its peak when

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infection is acquired at a late stage in gestation. (Congenital infection does not take place.[10])

Residual pulmonary coccidioidal lesions. Cavities may develop early in the course of the primary illness, often beginning within the pneumonic lesion a week or two after the onset of the disease. They occur in 2 to 8 per cent of symptomatic cases of pulmonary disease. On the other hand, the pneumonic areas may reduce in size to nodular or irregular residua over a period of weeks and months,[3] with occasional calcification of some of the lesions. The importance of these focalized residual lesions is that they persist for years and are the most common ones seen outside the endemic areas. For example, they have been noted in Vermont[11] and frequently in New York state.[12]

Thus, they must be considered in all localities in the differential diagnosis of chronic pulmonary disease, especially tuberculosis and neoplasm. Diagnosis can be established as follows:

History of residence or travel in certain areas. The disease is endemic in the arid southwestern states, California, New Mexico, Arizona, Texas, Utah and Nevada. Also, the spores of *Coccidioides immitis* are found in the soil of Mexico, Argentina and Venezuela and contaminate the air of mycologic laboratories containing cultures of the organism. Merely traveling on trains or riding through endemic areas in automobiles can produce infection.[2] Recently, a patient from Nova Scotia without contact with endemic areas was reported as having coccidioidomycosis.[13] This diagnosis was based on convincing pathological evidence, but the organism was not cultured. The author suggested that imported fruit was the source of infection.

Immunologic procedures. A positive coccidioidin skin test and a positive complement-fixation or precipitin reaction are of great diagnostic aid, especially if the tuberculin test is negative. Only 60 per cent of patients with coccidioidal cavities have a positive complement-fixation reaction.[2] Since the precipitin reaction becomes positive at about three weeks and reverts to negative by four months, it is better, in long-standing cases, to do only a complement-fixation test, which may remain positive for years.[3]

Roentgenologic findings. Jamison[14] discussed 96 pulmonary infections that persisted for months or years. The thin-walled cavities without surrounding infiltration are extremely suggestive of coccidioidal residua but are not diagnostic per se. Of these cavities, 90 per cent are single, and 70 per cent are located in the upper chest.[2] In addition, nodular foci are frequently noted, and, less often, enlarged mediastinal and hilar lymph nodes, miliary lung involvement, pleural effusion and persistent pneumonitis.

Repeated roentgenologic examination demonstrates that these solitary cavities and nodules may persist with little change for years,[12, 15] and this is an important diagnostic characteristic.

Culture. With asymptomatic coccidioidal pulmonary residua, sputum and gastric cultures are characteristically negative, and the handling of cultures on solid mediums almost invariably results in laboratory infections.[2, 16] However, the sputum can be positive, and cultures may be necessary in certain cases to establish the diagnosis. If suspicious cultures are obtained, they should be sent to laboratories properly equipped to handle them.

Surgery. Surgical exploration may be required to rule out cancer or tuberculosis.[17]

Prognosis and treatment. As mentioned above, a coccidioidal cavity signifies that dissemination will not take place, and when there are no complications a cavity is not an indication for thoracic surgery.

In a study of 92 cases of coccidioidal cavities, Winn[8] showed that 25 per cent closed spontaneously and 10 per cent persisted for years without harm. In 6 per cent the lesions filled and became solid foci resembling cancer. The remainder required surgery for various reasons. Greer[17] removed by wedge resection 4 focalized granulomas to rule out cancer, and performed lobectomies in 9 cases with cavities, chiefly because of repeated hemorrhage and infection. Occasionally, the cavities continue to increase in size and require pulmonary resection.[15] Persistent subpleural cavities should be removed surgically to prevent hydrothorax or pyopneumothorax.[3, 8] The consensus is that surgical treatment of these pulmonary residua has had excellent results without any evidence of dissemination. This is well substantiated by Cotton's[18] report on the surgical treatment in 30 cases of pulmonary coccidioidomycosis. It is important to stress again that, owing to modern transportation and travel, these pulmonary residua must be considered in the differential diagnosis of pulmonary lesions in all localities.[11, 12, 18]

Histoplasmosis

One of the outstanding advances in all medicine since 1945 has been the discovery of the common benign forms of histoplasmosis. A suggestion by Smith[19] initiated the epic work of Palmer[20] and Christie and Peterson.[21] It is now accepted that the classic course of histoplasmosis (Darling) with its widespread involvement of the reticuloendothelial system, depression of the blood elements, irregular fever, emaciation, and finally death, is the exception rather than the rule. Even while an unstable endemic area was being established in the Mississippi basin region, the disease was diagnosed in nontraveling natives of New York[22] and Vermont.[23] The organism, *Histoplasma capsulatum*, has been isolated from the soil of Detroit Lake, Minnesota, among other places.[24] Thus, histoplasmosis can be diagnosed in widespread localities where the index of suspicion is high and proper mycologic technics are utilized.

Histoplasmosis may be conveniently classified as pulmonary, both asymptomatic and symptomatic (nonepidemic and epidemic forms); disseminated (nonfatal and fatal); and localized (skin, penis, tongue and larynx).[25, 26]

Asymptomatic pulmonary histoplasmosis. Up to 1945 histoplasmosis was considered a routinely fatal disease, involving chiefly the reticuloendothelial system. At that time, Palmer[20] and, independently, Christie and Peterson[21] presented a plausible explanation for a well known enigma: the frequency of pulmonary calcification for different areas of the country varied at a rate that did not correspond to the incidence of tuberculosis in these areas, reaching its highest frequency in the central eastern part of the United States. In addition, pulmonary calcification was observed in negative tuberculin reactors; the explanation offered at that time was that the tuberculin sensitivity disappeared with healing by calcification. Then these investigators postulated that a benign asymptomatic form of pulmonary histoplasmosis existed, manifested by a positive skin test to histoplasmin and by pulmonary calcification. This assumption was based chiefly on the following facts: Palmer, in testing over 2000 nurses to both histoplasmin and tuberculin, noted that if they were negative to both histoplasmin and tuberculin, 1.2 per cent had pulmonary calcification; if positive to tuberculin alone, only 10.4 per cent, and if positive to histoplasmin alone, 31.1 per cent showed calcification. Also, the highest incidence of pulmonary calcification was found in the states bordering the Mississippi River and its larger tributaries — the exact area of highest histoplasmin reactors. This hypothesis was verified by various investigators,[27-30] and all agreed that pulmonary calcification was found twice as frequently with positive histoplasmin sensitivity as with positive tuberculin sensitivity. This held true even in Canada.[31] This benign asymptomatic form of histoplasmosis became an accepted fact with the observation of its clinical course from the onset of pulmonary infiltrate to the development of calcification in a histoplasmin-positive, tuberculin-negative reactor,[32] and finally with the isolation of *H. capsulatum* by culture in these cases.[33-35]

Symptomatic pulmonary histoplasmosis.

Nonepidemic form.[22, 23, 34-36] Histoplasmosis must be considered in the differential diagnosis of pulmonary disease resembling tuberculosis when repeated bacteriologic studies are negative for the tubercle bacillus. This is especially true if the tuberculin skin test is negative. Although cavities are rare, they have been present on several occasions.[22, 34-37] Also, one must consider the fact that the two diseases have frequently coexisted.[23, 36] Isolated cases with widespread miliary lesions have been noted,[36, 38] and are probably similar in all aspects to the epidemic form described below.

Epidemic form. Furcolow and Grayston[24, 39] have compiled about 200 cases of this form of pulmonary histoplasmosis, mainly by retrospective study of epidemics. From 1938 to 1951, a dozen different epidemics of acute widespread pulmonary disease were reported.[24] All presented similar clinical and roentgenologic findings, and most consisted of disseminated pneumonitis that tended to heal by eventual miliary calcification. The cause was unknown until recent years. Typical exposure histories are summarized as follows:

Nauen and Korns[40] described cases of "acute miliary pneumonitis" in 23 men who were engaged in shoveling pigeon manure from an old schoolhouse in Plattsburg, New York.

A similar history was presented by Feldman and Sabin[41] when a "pneumonitis of unknown etiology" occurred in 12 men shoveling a collection of pigeon manure from a basement of a water tower in Cincinnati.

Thirty-five soldiers contracted "an unusual pulmonary disease" after seeking shelter in a storm cellar during maneuvers in Oklahoma.[42]

Ten men acquired what was described as "angleworm pneumonia" while digging for fishing worms in Wisconsin.[24]

The first clue to this enigma came when Emmons[43] isolated *H. capsulatum* from the soil in 1949. Later, it was emphasized that the fungus was found much more frequently in soil contaminated with bird excreta.[44]

In 1950 White and Hill,[45] in a study of 114 cases of pulmonary calcification, suggested that *H. capsulatum* might be the causative agent of the previously described epidemics. This was based on a follow-up study of 10 of the cases of Nauen and Korns[40] in which disseminated pulmonary calcification, positive skin tests to histoplasmin and, in almost every case, positive complement-fixation titers subsequently developed. Schwartz and Spitz[46] came to a similar conclusion after study of 1 of the soldiers who acquired the disease in the storm cellar during maneuvers. The final proof came with the isolation of *H. capsulatum* from the soil at the point source of each of these epidemics[24, 39, 47] and from a patient with this disease.[45] Furcolow and Grayston[24, 39] have established the following criteria for diagnosis:

Isolation of *H. capsulatum* from the soil at the point source of the epidemic.

The presence of positive serologic tests for histoplasmosis.

The presence of positive histoplasmin skin tests.

The development of miliary calcification.

In their review of nearly 200 cases of acute, disseminated pneumonitis due to histoplasmosis, the symptomatology, course and roentgenologic findings present a remarkably constant picture. The incubation period was five to eighteen days. Onset was sudden, with generalized malaise, weakness, vague

chest pain, nonproductive cough and fever (temperature of 102° to 105°F.). There was a striking paucity of physical findings in all cases. X-ray examination of the chest during the first few days of the illness may be negative, followed by rapid development of extensive, diffuse, bilateral involvement. The disseminated lesions vary from fine, mottled, granular infiltrations to soft, miliary nodules. There is a marked tendency for eventual calcification to occur; this usually does not appear for four or five years after onset of illness. The course is variable, but is always associated with marked weight loss. Over 50 per cent of these patients had pulmonary symptoms lasting for years and consisting of dyspnea, cough and easy fatigability.[45]

Disseminated histoplasmosis — nonfatal form. It is only in the past few years that patients with proved cases of disseminated histoplasmosis have been known to survive, and several cases are now on record.[26, 38, 49] Wheeler[26] described simultaneous systemic histoplasmosis in 2 cousins, both of whom recovered. In 1 case the complement-fixation titer dropped from 1:1280 to 1:40 with resolution of the disease.

Localized histoplasmosis. Localized granulomas produced by histoplasmosis are reported most frequently on the penis, tongue, skin and larynx.[50-54] The lesions are misdiagnosed as syphilis, tuberculosis, leishmaniasis and neoplastic disease.

Raftery et al.[55, 56] state that histoplasmosis is a common cause of appendicitis and mesenteric adenitis, 5 per cent of appendixes being involved and 43 per cent of mesenteric lymph nodes. This is based on histologic evidence and one positive culture. Certainly, one could not make this diagnosis from the photomicrographs, and the observations have not been verified by subsequent investigators.[57]

Diagnosis. Diagnosis can be supported and established by direct examination of peripheral blood, bone marrow and sputum, by biopsy, culture, animal inoculation, skin tests and serologic and roentgenologic studies. All these methods, using the proper laboratory technics, may be required to arrive at the final diagnosis in a given case. For example, even when the vast majority of the cases studied were of the disseminated type, bone-marrow study produced a positive diagnosis in less than 50 per cent of the cases.[58] Routine histologic examination may fail to demonstrate the small intracellular yeast organisms[53]; also, some of the routine mycologic mediums may fail to effect culture of the fungus.[59]

Treatment. This varies with the clinical form present. Lobectomy has been successful in the rare localized forms of symptomatic pulmonary histoplasmosis.[36, 37] Otherwise, here and in the epidemic pulmonary form, prognosis is favorable with proper bed rest and nutrition.[22, 24, 39] In the disseminated type, quinacrine,[60] diethylstilbestrol,[61] antihistamines[62] and ethyl vanillate[63, 64] may be of value. The localized granulomas may disseminate,[52, 65] and probably surgical excision is the treatment of choice when possible.

North American Blastomycosis

Until the turn of this decade, systemic blastomycosis had a mortality of 92 per cent in patients who had been followed for two years or longer.[66] Now an aromatic diamidine, stilbamidine, is being used successfully in its treatment.[67-70]

Elson,[71] in 1945, first noted that propamidine, one of the aromatic diamidines, was effective in vitro against *Blastomyces dermatitidis* and even more so against *Sporotrichum schenckii.* This observation was followed by its use in the relatively benign cutaneous form of blastomycosis; applied locally, propamidine resulted in partial improvement.[67] Since the drug is too toxic to be given parenterally, Schoenbach et al.[6] first utilized another diamidine, stilbamidine, intravenously in a patient with systemic blastomycosis. The immediate therapeutic effect was excellent. A later report on 3 additional patients verified the effectiveness of stilbamidine in the treatment of systemic blastomycosis.[69] Curtis and Harrell,[70] in addition to reporting rapid improvement in 2 patients with systemic blastomycosis treated with stilbamidine, cured 2 men with cutaneous blastomycosis by the daily use of 3 mg. of diethylstilbestrol, which was chosen because of its chemical similarity to the aromatic diamidines. Harder[61] had previously demonstrated that diethylstilbestrol in a concentration of 1:100,000 prevented the growth of *B. dermatitidis* in vitro.

The aromatic diamidines have been used in the treatment of several thousand patients with trypanosomiasis, many of whom were poor risks. No deaths have been recorded from the drug.[70] It should be diluted before intravenous use to prevent nitritoid reactions. The amount of stilbamidine necessary for cure is not known, but probably a total dosage of 3 to 6 gm. administered in two or three courses is sufficient. This is best given by slow intravenous drip of 100 to 150 mg. in 1000 cc. of 5 per cent glucose solution. After daily treatment for about two weeks, there is a variable rest period before the second or third course is begun.

In a fairly high percentage of patients, two to five months after treatment with stilbamidine, a selective neuropathy involving the trigeminal nerve occurs. Progressive sensory changes, with dissociated anesthesia are noted. Touch sensation is lost, whereas pain, temperature and pressure sensory modalities are maintained. This may persist for years.[72]

Cryptococcosis

Evidence is beginning to accumulate that the initial infection with *Cryptococcus neoformans*, as well as with *B. dermatitidis*, is pulmonary, and that

asymptomatic and benign forms of these diseases may exist as in coccidioidomycosis and histoplasmosis.[73-76] Both *B. dermatitidis* and *C. neoformans* have been isolated from the soil[75, 77] and can thus be inhaled in the same manner as the spores of *H. capsulatum* and *C. immitis*.

Cox and Tolhurst,[74] in a superior book on the subject of human torulosis (cryptococcosis) with a report of 13 cases from Australia, state that the disease is frequently primary in the lungs. Convincing evidence is presented that the disease of the lungs may heal spontaneously and, since symptoms are slight, may be completely overlooked.

The authors also state that pulmonary torulosis is usually a chronic disease, sometimes preceding meningitis by several years. Emmons[75] concurs with these conclusions. Likewise, Schwarz and Baum[73] believe that, with blastomycosis, a tendency to heal is common in the lung. If these concepts are proved to be correct, it behooves the practitioner to be alert to diagnose the primary lesions, which are potentially curable by surgical and medical methods. Cryptococcus has such a strong predilection for the meninges that meningitis is its eventual common recognizable clinical form. At this stage the mortality approaches 100 per cent.[78]

The incidence of concomitant malignant lymphomas (chiefly Hodgkin's disease) in cryptococcosis and disseminated histoplasmosis is about 10 per cent.[79-81]

The association of these two systemic mycoses and Hodgkin's disease occurs much too frequently to be simply a matter of chance. It is doubtful if these fungi are of much significance in the etiology of malignant lymphomas.[79] Cox and Tolhurst[74] state that chronic cryptococcosis is associated with lymphadenopathy in 18 per cent of cases and that the lymph nodes may degenerate into malignant lymphomas, whereas Burger and Morton[82] have called attention to the fact that cryptococcosis produces granulomatous lesions resembling those of Hodgkin's disease. They postulate that perhaps some of the cases were misdiagnosed as Hodgkin's disease before the diagnosis of cryptococcosis was established. Another likely explanation for the close association of these diseases is an impaired immunologic response in patients with Hodgkin's disease.[83] The tuberculin skin test, known previously to be positive, becomes negative with the onset of this disease. Similar depression of serologic reactions for syphilis has been noted. Therefore, it may be postulated that the malignant lymphomas predispose to cryptococcosis and histoplasmosis on the basis of altered immunologic response on the part of the host. With these facts in mind, Ende et al.[81] have suggested that if a lymphoma is suspected, material from lymph-node biopsies should be routinely cultured for fungi.

Although most patients with cryptococcal meningitis die within six months, some survive this initial meningitic phase of the disease and have a partial remission lasting for two to four years.[84] Willard and Wolff[85] stress the fact that this course — the initial, severe meningitis followed by long remission and then a recurrence, with a rapid decline and death — is typical and diagnostic of cryptococcosis.

According to Neuhauser and Tucker,[86] when calcification of the brain is found by roentgenologic studies of newborn infants, central-nervous-system cryptococcosis must be considered in the differential diagnosis, as well as toxoplasmic encephalomyelitis. This is based on the study of 3 infants, all of whom died from cryptococcosis. Roentgenograms revealed punctate and confluent calcification scattered throughout the degenerated brain.

Treatment. Streptomycin-producing strains of *Streptomyces griseus* have been found to yield a second antibiotic, actidione. Of the fungal pathogens tested, only *C. neoformans* has proved highly sensitive to this antibiotic.[87, 88] Actidione has been used with partial success in the treatment of cryptococcal meningitis.[78, 89] Since *C. neoformans* does not survive an elevation of the body temperatures in mice,[90, 91] fever therapy is worthy of clinical trial as an adjuvant to actidione. Furthermore, because *C. neoformans* is highly sensitive to an alkaline pH,[92] investigative studies along this line might prove fruitful.

Surgical resection is probably the treatment of choice in pulmonary cryptococcosis. Baker[93] discussed successful resection in 3 cases and suggested that perhaps resection was prophylaxis against the development of cryptococcal meningitis.

South American Blastomycosis

Since the last Medical Progress report, further articles have confirmed the effectiveness of sulfonamides in the treatment of South American blastomycosis.[94, 95]

Mucormycosis, Aspergillosis and Geotrichosis

Aspergillosis[96-99] and geotrichosis[100, 101] have been the subject of several more reports. These nondescript pulmonary infections are difficult to prove even with a positive culture, because Aspergillus is a common laboratory contaminant, and Geotrichum is one of three potentially pathogenic fungi that are endogenous, the other two being *Actinomyces israeli* and *Candida albicans*. In almost all cases, *Aspergillus fumigatus* has been identified as the causative organism of aspergillosis, for which no effective treatment has been discovered to date. Neomycin has been effective against Geotrichum in vitro[102] and has been successfully employed in the treatment of 1 case of Geotrichum septicemia.[101]

On the other hand, the reports on mucormycosis, even though not confirmed by cultures, establish this as a definite clinical and pathological entity[103-106]: it occurs in patients with diabetes mellitus, chiefly uncontrolled cases; it is acutely fatal, most patients dying within a week of onset; pathologically,

vascular thrombi are produced by massive invasion of the blood-vessel walls by the fungous filaments; and, with central-nervous-system infection, there is infection of the orbit.[103, 104]

Actinomycosis and Nocardiosis

Acting as a stepping-stone between the bacteria and fungi are the genera Actinomyces, Nocardia and Streptomyces. This can best be demonstrated by use of a greatly simplified classification of the order Actinomycetales[107] as follows:

Group A. Mycelium (branched, elongated filaments) is rudimentary or absent. Genus: *Mycobacterium tuberculosis* and so forth.

Group B. Mycelium is present but segmented into bacillary and coccoid forms:

Anaerobic — nonacid fast (Genus: Actinomyces).

Aerobic — some species partly acid fast (Genus: Nocardia).

Group C. Mycelium is present and does not usually segment into bacillary and coccoid forms (Genus: Streptomyces).

By referring to this classification, one can follow the evolution from bacteria to fungi. In Group A the tubercle bacilli are found. Group B contains mycelia, some of which are not maintained but fragment into bacillary forms of the same size as the tubercle bacilli (1 millimicron). When some species of Nocardia are present that are acid fast, it is difficult to distinguish the bacillary forms from *Myco. tuberculosis*. Finally, mycelia are formed and maintained, furnishing the important soil fungus, Streptomyces. From this group, the present-day antibiotics — streptomycin, chlortetracycline, oxytetracycline, actidione and so forth — are derived.

Actinomycosis

This is one of the most common and best known of the systemic mycoses. Everyone is well acquainted with the cervicofacial, abdominal and pulmonary forms; but less is known of actinomycosis of the vertebral column, of the rectum and of the ovaries and fallopian tubes, even though excellent reports on these subjects have been published in recent years.

Actinomycosis of the vertebral column is covered in an excellent review of 66 cases by Cope.[108] This disease is always secondary to infection of contiguous tissue. It arises from deep cervical infection, an extending mediastinal infection, retroperitoneal infection after perforated appendicitis or perforated peptic ulcer. It is confused with tuberculosis of the spine, and differentiated from it by the following findings in actinomycosis: intervertebral disks are usually spared; transverse processes and heads of the neighboring ribs are often attacked; collapse of vertebral bodies and kyphosis are uncommon; and a latticework appearance on the roentgenogram is characteristic when present (if the entire vertebral body is involved, it is riddled by a network of suppurating channels, which are bounded by bone of increased density, a sort of honeycomb effect).

Cope[109] also discussed 40 cases of actinomycosis of the rectum. Half these cases began as primary lesions arising in the ampulla of the rectum. In the other 50 per cent, the disease was secondary to a focus elsewhere in the abdomen. The latter group presented the characteristic history of an acute condition of the abdomen, followed three to six months later by rectal symptoms. Primary actinomycosis of the rectum begins as a perianal or ischiorectal abscess. This bursts spontaneously and then becomes a subacute or chronic process. Extension of the disease is posteriorly and laterally rather than anteriorly, and thus it progresses into the gluteal region. Occasionally, a woody-hard lesion by the side of the rectum may be the presenting sign of this disease.

Paalman et al.[110] point out that there are over 100 cases of actinomycosis of the ovaries and tubes in the literature, and therefore every gynecologist should at least be aware of the disease. Although the history of previous abdominal surgical operations followed by signs and symptoms of pelvic inflammatory disease is suggestive, there is no specific clinical picture.

Putman, Dockerty and Waugh[111] have presented an excellent analysis of 122 cases of abdominal actinomycosis. Of the 122 patients, 103 had emergency surgical procedures for acute gastrointestinal lesions before the onset of actinomycosis. The typical operation was for acute appendicitis — usually with perforation. This preceded the abdominal actinomycosis in 88 cases.

Treatment. Penicillin in large daily dosage (1,000,000 units) continued without interruption for weeks is the treatment of choice. On occasion, however, this drug is not effective[112] or cannot be used because of penicillin sensitivity. Chlortetracycline,[113-115] chloramphenicol[112, 116] and streptomycin[117] have all been given successfully in the treatment of actinomycosis; in any case, however, it is best to culture the organism and perform sensitivity tests, because of variable species susceptibility.[118]

Nocardiosis

There are many valid reasons why this disease should become a clinical entity separate from actinomycosis. *Nocardia asteroides* is the principal causative organism of nocardiosis and, when present, differentiates the disease from actinomycosis as follows: nocardia is an exogenous fungus; sinuses are rare,[119] and even when exudate is examined, no clubs or granules are found[120]; Ziehl–Neelsen stains of direct specimens (sputum and so forth) reveal acid-fast bacilli or mycelia[120] or both; nocardia can be cultured aerobically; in tissue the fungal filaments are widely scattered, not aggregated into a "ray," and may not be demonstrated by means of hema-

toxylin and eosin preparations[119]; and sulfadiazine is the treatment of choice.

Clinically, nocardiosis is initially a pulmonary infection so closely simulating tuberculosis that the diagnosis of tuberculosis may be made.[121, 122] Nocardiosis may be quiescent until it gives rise to metastatic lesions, producing empyema, brain abscesses, subcutaneous abscesses, or, in addition, widely disseminated abscesses in liver, spleen, kidney, adrenal glands, intestinal walls and muscles. Many authors stress the point that the history of chronic pulmonary disease, followed by neurologic symptoms, places nocardiosis high in the list for differential diagnosis.[123-125]

Treatment. Sulfadiazine is the drug of choice in treatment, with antibiotic adjuvants as indicated by sensitivity tests.[118] Since Runyon[126] found a lack of correlation between protective and sensitivity tests in vivo (mice) and in vitro with the use of penicillin, chlortetracycline and sulfadiazine, and since the animal protective tests have been shown to be of greater value than in vitro sensitivity tests,[118] the animal protective tests may be necessary at times.

(To be concluded)

References

1. Downing, J. G., and Conant, N. F. Mycotic infections. *New Eng. J. Med.* **233**:153-161 and 181-188, 1945.
2. Smith, C. E. Diagnosis of pulmonary coccidioidal infections. *California Med.* **75**: 385-394, 1951.
3. Smith, C. E., Beard, R. R., and Saito, M. T. Pathogenesis of coccidioidomycosis with special reference to pulmonary cavitation. *Ann. Int. Med.* **29**:623-655, 1948.
4. Forbus, W. D., and Bestebreurtje, A. M. Coccidioidomycosis: study of 95 cases of disseminated type with special reference to pathogenesis of disease. *Mil. Surgeon* **99**:653-719, 1946.
5. Jenkins, V. E., and Postlewaite, J. C. Coccidioidal meningitis: report of four cases with necropsy findings in three cases. *Ann. Int. Med.* **35**:1068-1084, 1951.
6. Winer, L. H. Histopathology of nodose lesion of acute coccidioidomycosis. *Arch. Dermat. & Syph.* **61**:1010-1024, 1950.
7. Gifford, M. A., Buss, W. C., and Douds, R. J. Data on coccidioides fungus infection. In *Kern County Health Department Annual Report.* Bakersfield, California, 1936-1937.
8. Winn, W. A. Pulmonary mycoses — coccidioidomycosis and pulmonary cavitation: study of ninety-two cases. *Arch. Int. Med.* **87**: 541-550, 1951.
9. Buss, W. C., Gibson, T. E., and Gifford, M. A. Coccidioidomycosis of meninges. *California Med.* **72**:167-169, 1950.
10. Vaughan, J. E., and Ramirez, H. Coccidioidomycosis as complication of pregnancy. *California Med.* **74**:121-125, 1951.
11. Kurz, E. R. H., and Loud, N. W. Coccidioidomycosis in New England. *New Eng. J. Med.* **237**:610-616, 1947.
12. Bass, H. E., Schomer, A., and Berke, R. Coccidioidomycosis: persistence of residual pulmonary lesions. *Arch. Int. Med.* **82**:519-528, 1948.
13. McLetchie, N. G. B., Reid, N., and Simpson, D. M. Coccidioidomycosis. *Canad. M. A. J.* **67**:655-658, 1952.
14. Jamison, H. W. Roentgen study of chronic pulmonary coccidioidomycosis. *Am. J. Roentgenol.* **55**:396-412, 1946.
15. Weisel, W., and Owen, G. C. Pulmonary resection for coccidioidomycosis; report of case. *J. Thoracic Surg.* **18**:674-678, 1949.
16. Looney, J. M., and Stein, T. Coccidioidomycosis: hazard involved in diagnostic procedures, with report of cases. *New Eng. J. Med.* **242**:77-82, 1950.
17. Greer, S. J., Forsee, J. H., and Mahon, H. W. Surgical management of pulmonary coccidioidomycosis in focalized lesions. *J. Thoracic Surg.* **18**:591-604, 1949.
18. Cotton, B. H., and Birsner, J. W. Surgical treatment in pulmonary coccidioidomycosis: preliminary report of thirty cases. *J. Thoracic Surg.* **20**:429-443, 1950.
19. Smith, C. E. Coccidioidomycosis. *M. Clin. North America* **27**:790 807, 1943.
20. Palmer, C. E. Nontuberculous pulmonary calcification and sensitivity to histoplasmin. *Pub. Health Rep.* **60**:513-520, 1945.
21. Christie, A., and Peterson, J. C. Pulmonary calcification in negative reactors to tuberculin. *Am. J. Pub. Health* **35**:1131-1147, 1945.
22. Monroe, J., and Kurung, J. M. Histoplasmosis, with review of literature and report of case, proved by culture, with involvement of upper lobe of each lung simulating active bilateral apical pulmonary tuberculosis. *Ann. Int. Med.* **38**:206-223, 1953.
23. French, E. E., Jillson, O. F., and Crispell, L. S. Histoplasmosis in life-long resident of New England. *New Eng. J. Med.* **249**:270-272, 1953.
24. Furcolow, M. L., and Grayston, J. T. Nontuberculous chest diseases: occurrence of histoplasmosis in epidemics. *Nat. Tuberc. A. Tr.* **48**:83-91, 1952.
25. Beadenkopf, W. G., and Loosli, C. G. Histoplasmosis, tuberculosis and coccidioidomycosis. *J. A. M. A.* **146**:621-624, 1951.
26. Wheeler, W. E., Friedman, V., and Saslaw, S. Simultaneous nonfatal systemic histoplasmosis in two cousins. *Am. J. Dis. Child.* **79**:806-819, 1950.
27. Beadenkopf, W. G., Loosli, C. G., Lack, H., Rice, F. A., and Slattery, R. V. Tuberculin, coccidioidin and histoplasmin sensitivity in relation to pulmonary calcifications: survey among 6,000 students at University of Chicago. *Pub. Health Rep.* **64**:17-32, 1949.
28. Smith, C. E., Saito, M. T., Beard, R. R., Rosenberger, H. G., and Whiting, E. G. Histoplasmin sensitivity and coccidioidal infection. I. Occurrence of cross-reactions. *Am. J. Pub. Health* **39**:722-736, 1949.
29. Mochi, A., and Edwards, P. Q. Geographical distribution of histoplasmosis and histoplasmin sensitivity. *Bull. World Health Organ.* **5**:259-291, 1952.
30. Loosli, C. G., Beadenkopf, W. G., Rice, F. A., and Savage, L. J. Epidemiological aspects of histoplasmin, tuberculin, and coccidioidin sensitivity. *Am. J. Hyg.* **53**:33-57, 1951.
31. Green, P. Pulmonary calcification and histoplasmin sensitivity. *Canad. M. A. J.* **63**:143-146, 1950.
32. Furcolow, M. L. Development of calcification in pulmonary lesions associated with sensitivity to histoplasmin. *Pub. Health Rep.* **64**: 1363-1393, 1949.
33. Kunstadter, R. H., Whitcomb, F. C., and Milzer, A. Primary histoplasmosis with recovery of histoplasma capsulatum from blood and bronchial secretions. *J. Lab. & Clin. Med.* **34**:1290-1297, 1949.
34. Furcolow, M. L. Further observations on histoplasmosis: mycology and bacteriology. *Pub. Health Rep.* **65**:965-994, 1950.
35. Johnson, H. E., and Batson, R. Benign pulmonary histoplasmosis: case report with brief review of literature. *Dis. of Chest* **14**:517-524, 1948.
36. Hodgson, C. H., Weed, L. A., and Clagett, O. T. Pulmonary histoplasmosis: summary of data on reported cases and report on two patients treated by lobectomy. *J. A. M. A.* **145**:806-810, 1951.
37. Bettag, O. L. Pulmonary resection for histoplasmosis. *J. Thoracic Surg.* **22**:434-438, 1951.
38. Bunnell, I. L., and Furcolow, M. L. Report on ten proved cases of histoplasmosis. *Pub. Health Rep.* **63**:299-316, 1948.
39. Grayston, J. T., and Furcolow, M. L. Acute febrile illness with disseminated pulmonary infiltrations: syndrome caused by Histoplasma capsulatum. *Tuberculology*, September, 1952. Pp. 1-6.
40. Nauen, R., and Korns, R. F. Localized epidemic of acute miliary pneumonitis, associated with handling of pigeon manure. Presented at the Seventy-Third Annual Meeting of the American Public Health Association, New York, October 3, 1944.
41. Feldman, H. A., and Sabin, A. B. Pneumonitis of unknown etiology in group of men exposed to pigeon excreta. *J. Clin. Investigation* **27**:533, 1948.
42. Cain, J. C., Devine, E. J., and Downing, J. E. Unusual pulmonary disease. *Arch. Int. Med.* **79**:626-641, 1947.
43. Emmons, C. W. Isolation of *Histoplasma capsulatum* from soil. *Pub. Health Rep.* **64**:892-896, 1949.
44. Zeidberg, L. D., Ajello, L., Dillon, A., and Runyon, L. C. Isolation of *Histoplasma capsulatum* from soil. *Am. J. Pub. Health* **42**:930-935, 1952.
45. White, F. C., and Hill, H. E. Disseminated pulmonary calcification: report of 114 cases with observations of antecedent pulmonary disease in 15 individuals. *Am. Rev. Tuberc.* **62**:1-16, 1950.
46. Schwartz, B., and Spitz, L. J. Histoplasmosis in epidemic form. *Arch. Int. Med.* **89**:541-546, 1952.
47. Furcolow, M. L., and Larsh, H. W. Direct isolation of *Histoplasma capsulatum* from soil: probable etiological relationship to Camp Gruber pneumonitis. *Proc. Soc. Exper. Biol. & Med.* **80**:246-248, 1952.
48. Loosli, C. G., Grayston, J. T., Alexander, E. R., and Tanzi, F. Epidemiological studies of pulmonary histoplasmosis in farm family. *Am. J. Hyg.* **55**:392-401, 1952.
49. Blumberg, R. W., Ruchman, I., and Johansmann, R. J. Generalized nonfatal histoplasmosis in infant. *Pediatrics* **3**:296-302, 1949.
50. Parsons, R. J., and Zarafonetis, C. J. D. Histoplasmosis in man: report of seven cases and review of seventy-one cases. *Arch. Int. Med.* **75**:1-23, 1945.
51. Curtis, A. C., and Cawley, E. P. Genital histoplasmosis. *J. Urol.* **57**:781-787, 1947.
52. Curtis, A. C., and Grekin, J. N. Histoplasmosis: review of cutaneous and adjacent mucous membrane manifestations with report of three cases. *J. A. M. A.* **134**:1217-1224, 1947.
53. Weed, L. A., and Parkhill, E. M. Diagnosis of histoplasmosis in ulcerative disease of mouth and pharynx. *Am. J. Clin. Path.* **18**: 130-140, 1948.
54. Seabury, J. H. Stilbamidine in treatment of histoplasmosis: two case reports. *Ann. Int. Med.* **31**:520-523, 1949.
55. Raftery, A., Trafas, P. C., and McClure, R. D. Histoplasmosis: common cause of appendicitis and mesenteric adenitis. *Ann. Surg.* **132**:720-728, 1950.
56. Raftery, A. Subclinical histoplasmosis: gastrointestinal histoplasmosis of children. *J. A. M. A.* **145**:216-219, 1951.
57. Christopherson, W. M., Miller, M. P., and Kotcher, E. Examination of human appendixes for *Histoplasma capsulatum*. *J. A. M. A.* **149**:1648, 1952.

58. Pratt, P. T., Schwartz, S. O., and Erlich, L. Aspiration biopsy of bone marrow as aid in diagnosis of histoplasmosis: report of case. *Arch. Int. Med.* **85**:893-899, 1950.
59. Howell, A. Efficiency of methods for isolation of *Histoplasma capsulatum*. *Pub. Health Rep.* **63**:173-178, 1948.
60. Campbell, C. C., and Saslaw, S. Atabrine therapy of histoplasma infections in mice. *Pub. Health Rep.* **66**:570-577, 1951.
61. Harder, F. K. Antimycotic effect of diethylstilbestrol. *North Carolina M. J.* **7**:20-22, 1946.
62. Carson, L. E., and Campbell, C. C. Inhibitory effect of three antihistaminic compounds on growth of fungi pathogenic for man. *Science* **111**:689-691, 1950.
63. Hansen, A. E., and Beene, M. L. Sensitivity studies *in vitro* with *Histoplasma capsulatum* to various potential therapeutic agents. *Proc. Soc. Exper. Biol. & Med.* **77**:365, 1951.
64. Christie, A., Middleton, J. G., Peterson, J. C., and McVickar, D. L. Treatment of disseminated histoplasmosis with ethyl vanillate. *Pediatrics* **7**:7-18, 1951.
65. Palmer, A. E., Amolsch, A. L., and Shaffer, L. W. Histoplasmosis with mucocutaneous manifestations. *Arch. Dermat. & Syph.* **45**: 912-916, 1942.
66. Martin, D. S., and Smith, D. T. Blastomycosis (American blastomycosis, Gilchrist's disease). I. Review of literature. *Am. Rev. Tuberc.* **39**:275-304, 1939. II. Report of 13 new cases. *Ibid.* **39**: 488-515, 1939.
67. Colbert, J. W. Jr., Strauss, M. J., and Green, R. H. Treatment of cutaneous blastomycosis with propamidine: preliminary report. *J. Invest. Dermat.* **14**:71-73, 1950.
68. Schoenbach, E. B., Miller, J. M., Ginsberg, M., and Long, P. H. Systemic blastomycosis treated with stilbamidine. *J. A. M. A.* **146**:1317, 1951.
69. Schoenbach, E. B., Miller, J. M., and Long, P. H. Treatment of systemic blastomycosis with stilbamidine. *Ann. Int. Med.* **37**: 31-47, 1952.
70. Curtis, A. C., and Harrell, E. R., Jr. Use of two stilbene derivatives (diethylstilbestrol and stilbamidine) in treatment of blastomycosis. *Arch. Dermat. & Syph.* **66**:676-690, 1952.
71. Elson, W. O. Antibacterial and fungistatic properties of propamidine. *J. Infect. Dis.* **76**:193-197, 1945.
72. Schoenbach, E. B., and Greenspan, E. M. Pharmacology, mode of action and therapeutic potentialities of stilbamidine, pentamidine, propamidine and other aromatic diamidines. *Medicine* **27**:327-377, 1948.
73. Schwarz, J., and Baum, G. L. Blastomycosis. *Am. J. Clin. Path.* **21**:999-1029, 1951.
74. Cox, L. B., and Tolhurst, J. C. *Human Torulosis: A clinical, pathological and microbiological study, with a report of 13 cases.* 149 pp. Melbourne: Melbourne Univ. Press, 1946.
75. Emmons, C. W. Isolation of Cryptococcus neoformans from soil. *J. Bact.* **62**:685-690, 1951.
76. Greening, R. R., and Menville, L. J. Roentgen findings in torulosis: report of four cases. *Radiology* **48**:381-387, 1947.
77. Emmons, C. W. Isolation from soil of fungi which cause disease in man. *Tr. New York Acad. Sc.* **14**:51-54, 1951.
78. Carton, C. A. Treatment of central nervous system cryptococcosis: review and report of four cases treated with actidione. *Ann. Int. Med.* **37**:123-134, 1952.
79. Gendel, B. R., Ende, M., and Norman, S. L. Cryptococcosis: review with special reference to apparent association with Hodgkin's disease. *Am. J. Med.* **9**:343-355, 1949.
80. Murray, J. F., and Brandt, F. A. Histoplasmosis and malignant lymphoma. *Am. J. Path.* **27**:783-799, 1951.
81. Ende, M., Pizzolato, P., and Ziskind, J. Hodgkin's disease associated with histoplasmosis. *Cancer* **5**:763-769, 1952.
82. Burger, R. E., and Morton, C. B. Torula infection: review and report of four cases. *Surgery* **15**:312-325, 1944.
83. Dubin, I. N. Poverty of immunological mechanism in patients with Hodgkin's disease. *Ann. Int. Med.* **27**:898-913, 1947.
84. Voyles, G. Q., and Beck, E. M. Systemic infection due to Torula histolytica (Cryptococcus hominis): report of 4 cases and review of literature. *Arch. Int. Med.* **77**:504-515, 1946.
85. Willard, H. N., and Wolff, H. G. Remission as feature in torulosis. *J. Nerv. & Ment. Dis.* **112**:237-239, 1950.
86. Neuhauser, E. B. D., and Tucker, A. Roentgen changes produced by diffuse torulosis in newborn. *Am. J. Roentgenol.* **59**:805-815, 1948.
87. Whiffen, A. J., Bohonos, N., and Emerson, R. L. Production of antifungal antibiotic by Streptomyces griseus. *J. Bact.* **52**:610, 1946.
88. Leach, B. E., Ford, J. H., and Whiffen, A. J. Actidione, antibiotic from Streptomyces griseus. *J. Am. Chem. Soc.* **69**:474, 1947.
89. Wilson, H. M., and Duryea, A. W. Cryptococcus meningitis (torulosis) treated with new antibiotic, actidione. *Arch. Neurol. & Psychiat.* **66**:470-480, 1951.
90. Kuhn, L. R. Effect of elevated body temperatures on cryptococcosis in mice. *Proc. Soc. Exper. Biol. & Med.* **71**:341-343, 1949.
91. Kligman, A. M., and Weidman, F. D. Experimental studies on treatment of human torulosis. *Arch. Dermat. & Syph.* **60**:726-741, 1949.
92. Mosberg, W. H., and Alvarez-DeChoudens, J. A. Torulosis of central nervous system: effect of changes in pH and temperature on growth of causal organism. *Lancet* **1**:1259, 1951.
93. Baker, R. D. Resectable mycotic lesions and acutely fatal mycoses. *J. A. M. A.* **150**:1579-1581, 1952.
94. Negroni, P. Sobre el tratamiento de la blastomicosis sudamericana: a propósito de dos nuevas observaciones. *Rev. argent. dermatosif.* **30**:223-228, 1946.
95. Monteiro de Barros, O. Sur la maladie de Lutz, Splendore et Almeida. *Bull. Soc. path. exot.* **43**:114-120, 1950.
96. Cawley, E. P. Aspergillosis and aspergilli: report of unique case of disease. *Arch. Int. Med.* **80**:423-434, 1947.
97. Cooper, N. S. Acute bronchopneumonia due to Aspergillus fumigatus Fresenius: report of case with description of acute and granulomatous lesions produced by fungus in rabbits. *Arch. Path.* **42**:644-648, 1946.
98. Gerstl, B., Weidman, W. H., and Newmann, A. V. Pulmonary aspergillosis: report of two cases. *Ann. Int. Med.* **28**:662-671, 1948.
99. Hertzog, A. J., Smith, T. S., and Goblin, M. Acute pulmonary aspergillosis. *Pediatrics* **4**:331-335, 1949.
100. Kunstadter, R. H., Milzer, A., and Whitcomb, F. C. Bronchopulmonary geotrichosis in children. *Am. J. Dis. Child.* **79**:82-90, 1950.
101. Bendove, R. A., and Ashe, B. I. Geotrichum septicemia. *Arch. Int. Med.* **89**:107-110, 1952.
102. Duncan, G. G., Clancy, C. F., Wolgamot, J. R., and Beidleman, B. Neomycin: results of clinical use in ten cases. *J. A. M. A.* **145**:75-80, 1951.
103. Gregory, J. E., Golden, A., and Haymaker, W. Mucormycosis of central nervous system: report of three cases. *Bull. Johns Hopkins Hosp.* **73**:405-419, 1943.
104. LeCompte, P. M., and Meissner, W. A. Mucormycosis of central nervous system associated with hemochromatosis. *Am. J. Path.* **23**:673-677, 1947.
105. Baker, R. D., and Severance, A. O. Mucormycosis; with report of acute mycotic pneumonia. *Am. J. Path.* **24**:716, 1948.
106. Lloyd, J. B., Sexton, L. I., and Hertig, A. T. Pulmonary mucormycosis complicating pregnancy. *Am. J. Obst. & Gynec.* **58**:548-552, 1949.
107. Waksman, S. A., and Henrici, A. T. Nomenclature and classification of Actinomycetes. *J. Bact.* **46**:337-341, 1943.
108. Cope, V. Z. Actinomycosis of bone with special reference to infection of vertebral column. *J. Bone & Joint Surg.* **33B**:205-214, 1951.
109. *Idem.* Actinomycosis involving rectum and colon. *Proc. Roy. Soc. Med.* **42**:763-768, 1949.
110. Paalman, R. J., Dockerty, M. B., and Mussey, R. D. Actinomycosis of ovaries and fallopian tubes. *Am. J. Obst. & Gynec.* **58**:419-431, 1949.
111. Putman, H. C., Jr., Dockerty, M. B., and Waugh, J. M. Abdominal actinomycosis: analysis of 122 cases. *Surgery* **28**:781-800, 1950.
112. Littman, M. L., Phillips, G. E., and Fusillo, M. H. In vitro susceptibility of human pathogenic actinomycetes to chloramphenicol (chloromycetin). *Am. J. Clin. Path.* **20**:1076-1078, 1950.
113. McVay, L. V., Dunavant, D., Guthrie, F., and Sprunt, D. H. Treatment of actinomycosis with aureomycin: report of case. *J. A. M. A.* **143**:1057, 1950.
114. McVay, L. V., Guthrie, F., and Sprunt, D. H. Aureomycin in treatment of actinomycosis. *New Eng. J. Med.* **245**:91-96, 1951.
115. Wright, L. T., and Lowen, H. J. Aureomycin hydrochloride in actinomycosis. *J. A. M. A.* **144**:21, 1950.
116. Littman, M. L., Paul, J. S., and Fusillo, M. H. Treatment of pulmonary actinomycosis with chloramphenicol. *J. A. M. A.* **148**:608-612, 1952.
117. Torrens, J. A., and Wood, M. W. W. Streptomycin in treatment of actinomycosis: report on three cases. *Lancet* **256**:1091-1094, 1949.
118. Strauss, R. E., Kligman, A. M., and Pillsbury, D. M. Chemotherapy of actinomycosis and nocardiosis. *Am. Rev. Tuberc.* **63**:441-448, 1951.
119. Kirby, W. M. M., and McNaught, J. B. Actinomycosis due to Nocardia asteroides: report of two cases. *Arch. Int. Med.* **78**:578-591, 1946.
120. Hager, H. F., Migliaccio, A. V., and Young, R. M. Nocardiosis: pneumonia and empyema due to Nocardia asteroides. *New Eng. J. Med.* **241**:226-231, 1949.
121. Glover, R. P., Herrell, W. E., Heilman, F. R., and Pfuetze, K. H. Nocardiosis: Nocardia asteroides infection simulating pulmonary tuberculosis. *J. A. M. A.* **136**:172-175, 1948.
122. Mogabgab, W. J., and Floyd, J. L. Acid-fast Nocardia causing erroneous diagnosis of tracheobronchial tuberculosis. *New Orleans M. & S. J.* **104**:28-31, 1951.
123. Binford, C. H., and Lane, J. D. Actinomycosis due to Nocardia asteroides. *Am. J. Clin. Path.* **15**:17-23, 1945.
124. Bernstein, I. L., Cook, J. E., Plotnick, H., and Tenczar, F. J. Nocardiosis: three case reports. *Ann. Int. Med.* **36**:852-863, 1952.
125. Tucker, F. C., and Hirsch, E. F. Nocardiosis, with report of three cases of actinomycosis due to Nocardia asteroides. *J. Infect. Dis.* **85**:72-86, 1949.
126. Runyon, E. H. Nocardia asteroides: studies of its pathogenicity and drug sensitivities. *J. Lab. & Clin. Med.* **37**:713-720, 1951.

MEDICAL INTELLIGENCE

JAPANESE B ENCEPHALITIS IN AN AMERICAN SOLDIER RETURNING FROM KOREA

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TO the best of our knowledge, no case of Japanese B encephalitis has previously been reported as occurring in personnel among Far East troops after evacuation to the United States. That this possibility is not far fetched is illustrated by the case reported below. Rapid evacuation by air from an endemic or epidemic zone of Japanese B encephalitis may result in recognition of other cases of this type in the continental United States.

CASE REPORT

A 25-year-old sergeant was admitted to Murphy Army Hospital on September 13, 1952, while on leave. His chief complaints were headache, beginning 4 days before admission, and progressive lethargy and confusion.

The past history was irrelevant except for indigestion 4 years previously. There was no history of mental disorder. The family history was negative for mental disease and epilepsy.

The patient had been in Korea since June 1, 1951. He was stationed near Seoul in an antiaircraft battery until August, 1952. On August 8 he left Korea by ship, arriving the next morning at the Port of Sasabo in southern Japan. He was there for 2 weeks and then went to Tokyo, where he arrived on August 22. He left Tokyo by plane 1 week later and landed at Travis Air Force Base, San Francisco, on August 30. He remained in San Francisco until September 4, when he left by plane for Massachusetts, arriving at Worcester on September 7. During all this time, he was in excellent health. He did not remember exposure to any disease or insect bites of any kind. After arriving home on September 9 he complained of a mild headache. That night he also felt somewhat chilly. On the next morning when he awoke he felt somewhat sluggish, slightly nauseated and drowsy, these symptoms continuing for most of the day. He had to be awakened for meals. His temperature was recorded at between 101 and 103°F. His family physician, who was called that day, made a diagnosis of virus infection. Chlortetracycline was prescribed. On September 11 he was still lethargic and then became mentally confused and disoriented. On the following day he was seen by another physician, who agreed with the previous diagnosis and gave him penicillin, by injection. He did not have any shaking chills, sweats or marked weakness. There was no vomiting. There was no sore throat, cold, cough, earache, ear discharge, joint pains or urinary symptoms. He was admitted to Murphy Army Hospital on September 13. On admission, he was mentally confused and was unable to give any coherent history. However, information was elicited as above, partly from his relatives and partly from the patient after recovery from his acute illness.

Physical examination showed a well developed, well nourished man lying quietly in bed. The mental state was quite confused. He knew his name, but was disoriented concerning time and place. He was somewhat euphoric but tended to be lethargic when left alone. When questioned at first he stated that he had never been out of the United States. Later, he was not sure whether he had been in Korea. Attention was poorly maintained. Neurologic examination demonstrated questionable minimal narrowing of the left palpebral fissure, but the cranial nerves were otherwise intact. There was no motor weakness or paralysis. Sensory reactions to pain, pressure and position were grossly intact. The deep tendon reflexes were active and equal bilaterally. Abdominal and cremasteric reflexes were also equal and active. Co-ordination, heel-to-toe and finger-to-nose tests were well accomplished bilaterally. The neck was not stiff, but there was some resistance to extreme anteflexion. The back was not stiff. The Kernig sign was borderline bilaterally, with some hamstring tightness. The lungs were clear. The heart was normal except for a soft, Grade 1 systolic mitral murmur. The skin showed no petechiae or ecchymoses.

The temperature was 103.2°F., the pulse 106, and the blood pressure 115/60.

The initial clinical diagnosis was acute encephalitis of undetermined etiology (? Japanese B) and a question of brain abscess.

Examination of the blood revealed a hemoglobin of 12.5 gm. per 100 cc. and a white-cell count of 18,500, with 82 per cent neutrophils, 10 per cent lymphocytes, 5 per cent monocytes, 2 per cent eosinophils and 1 per cent basophils. A blood smear was negative for malarial parasites. Urinalysis on September 14 was entirely normal, with a specific gravity of 1.005. The spinal fluid had a cell count of 176 per cubic millimeter with 81 per cent polymorphonuclear leukocytes, 19 per cent lymphocytes and a total protein of 43 mg. per 100 cc.; smear showed no organisms. The initial spinal-fluid pressure was equivalent to 240 mm., and the final pressure to 140 mm. of water. Examination of the blood on September 15 demonstrated a hemoglobin of 12.9 gm. per 100 cc. and a white-cell count of 9250, with 80 per cent neutrophils, 18 per cent lymphocytes and 2 per cent monocytes. The erythrocyte sedimentation rate was 30 mm. per hour. On September 16 the blood urea nitrogen was 15 mg. per 100 cc. A repeat spinal fluid on September 17 disclosed a cell count of 97 per cubic millimeter, with 78 per cent leukocytes and 22 per cent lymphocytes; the sugar was 67 mg., the chloride 791 mg., and the total protein 41 mg. and culture was negative. On September 20 the cell count was 54 per cubic millimeter, with 49 polymorphonuclear leukocytes and 5 lymphocytes and a total protein of 36 mg. per 100 cc.; culture was negative. On September 29 the spinal-fluid cell count was 31 per cubic millimeter with 20 polymorphonuclear leukocytes and 11 lymphocytes; the sugar was 67 mg., the chloride 712 mg., and the total protein 41 mg. per 100 cc. Cardiolipin complement fixation was negative; the colloidal gold was 0000000000. A serologic test for syphilis was negative.

Serial studies for Japanese B encephalitis antibodies were done on specimens of serum drawn on 3 different days. Table 1 presents a summary of the report received from First Army

TABLE 1. *Summary of Tests for Japanese B Encephalitis.*

DATE OF SERUM	DAY OF ILLNESS	COMPLEMENT-FIXATION TEST	NEUTRALIZATION TEST
Sept. 16, 1952	7	Negative (1:4 titer)	4.1 logs*
Oct. 2, 1952	23	Positive (1:16 titer)	—
Oct. 16, 1952	37	Positive (1:32 titer)	3.7 logs*

*Antibodies expressed as logarithm of neutralization index.

Laboratory. The demonstration of a progressive increase in complement-fixing antibodies for Japanese B encephalitis from nondetectable amounts in the 7-day serum to significant levels in the 37-day serum is diagnostic of recent infection with this agent. The presence of neutralizing antibodies against the agent at high levels in the 7-day serum and persistence at essentially the same levels without a further increase in the 37-day serum is somewhat unusual in cases of Japanese B encephalitis. However, there is sufficient evidence that neutralizing antibodies against the virus may appear abruptly and rise to high levels shortly after the onset of clinical disease. The serologic findings, therefore, were regarded as establishing a diagnosis of Japanese B encephalitis.

X-ray films of the chest on September 19 and November 29 were normal, as were films of the skull taken on September 24. An upper gastrointestinal barium series was attempted on October 9, but the patient was emotionally disturbed throughout

*Formerly, chief, Communicable Diseases Section, Murphy Army Hospital.

†Chief, Medical Service, Murphy Army Hospital.

examination, with some nausea, so that examination was unsatisfactory.

Electroencephalograms* on September 15 were interpreted as revealing waves of 2 to 4 per second, with moderate high voltage and irregular, slow activity in all leads. There were slightly higher voltages on the left. The impression was of an abnormal tracing and a diffuse slightly more abnormal tracing on the left.

Repeat records on September 24 and October 15 showed similarly abnormal patterns. The last electroencephalogram, taken on December 3, was only minimally abnormal.

After the initial diagnostic studies, the patient was treated with chlortetracycline, 0.5 gm. every 6 hours, by mouth, and procaine-penicillin, 300,000 units intramuscularly, every 12 hours. He was also given fluids intravenously in the form of 5 per cent glucose in water. The temperature remained at 103°F. on the day of admission. On the following day it dropped to 101°F. in the morning but rose again to 103°F. in the evening. On the 3d hospital day, it remained at a level of 101°F., gradually dropping to 99.0°F. by the 6th hospital day and remaining at that level until the 10th hospital day. Subsequently, it was consistently at normal levels. During the first week in the hospital, the patient remained disoriented and mentally confused. He was moderately lethargic during the day. During the night, he required careful watching because he got up in a confused state and attempted to get out of bed without assistance. His appetite was poor, and he required help with food and fluids. In the 2d week he appeared to be a little clearer mentally and recognized his parents and sister, but remained disoriented concerning time and place. He occasionally vomited his breakfast in the morning. He had gross impairment of memory for recent and remote events. There were no neurologic changes of note. At no time during the hospital course did he complain of headache. By the 3d hospital week, he was much more alert and clearer mentally. By this time, he was fairly well oriented concerning time and persons; he was ambulatory and had absolutely no complaints. After approximately 1 month in the hospital he was allowed to go home on sick leave for 2 weeks. When he returned, he had no complaints, and there were no neurologic abnormalities. He was granted an additional 2 weeks of leave, from which he returned without complaints. His mental condition was entirely normal at this time. He had recovered his memory for almost all recent and remote events and was able to give all the detailed information recorded in the history. However, a memory block for the events during the first 2 weeks of the hospital admission persisted. He stated that he could not recollect any of the incidents connected with this period. He had gained weight; he no longer vomited in the morning and, according to the statement of himself and his friends, appeared to be his old self.

Neurologic examination was entirely negative. Lumbar puncture was entirely normal.

It is believed that this patient has made a complete recovery from the episode of acute encephalitis. His required period of military service has expired, and he has been discharged to civilian life.

Discussion

The incubation period of Japanese B encephalitis is said to be unknown, but estimated at about a week.† That it may be longer than this is indicated by the case presented above. If this soldier acquired his infection in Japan, the incubation period was at least thirteen days. If the disease was acquired in Korea, the incubation period was at least thirty-three days. We have no evidence for either of these alternatives.

Summary

A case of Japanese B encephalitis occurring in an American soldier evacuated from Korea via Japan is reported.

The diagnosis was confirmed by serial serologic tests.

*Interpreted by Commander John E. Nardini, MC, USN, chief of neuropsychiatry, Chelsea Naval Hospital.

†*Viral and Rickettsial Infections of Man.* Edited by T. M. Rivers. 587 pp. Philadelphia: Lippincott, 1948.

BY THE LONDON POST

Emancipation of Nurses — Medical Exhibitions — Postscript

John Lister, M.D.

London, England

THE emancipation of the hospital nurse has lagged far behind that of the rest of her sex. Not so long ago the nursing student was not allowed to speak to the medical student in the ward except when the conversation strictly concerned the patient. The ward sister (head nurse) was normally regarded as the spoil sport who could arrange to have moved to another part of the hospital any student nurse who appeared too friendly with one of the doctors and who would ensure that the regulations concerning the headgear and dress of her nurses were enforced so that the minimal degree of glamor could survive. Such usually unesthetic duties as the testing of urines and the inspection of patients' stools became the most enticing pastimes when they afforded the chance of five or even ten minutes in the sluice room, where a date could be planned away from sister's prying eyes. And yet all danger was not past, for a rendezvous had to be planned some distance from the nurses' home, and even when the evening began, its end was only a few hours off since all nurses returning to the Home after 10 o'clock were reported to the matron.

Bit by bit the restrictions have been broken (not that they were ever effective, for what is more attractive than that which is forbidden?), and at last the Minister of Health has issued an edict. Some time ago he appointed an advisory committee to consider whether there were any factors that made it necessary for nurses to live in the hospital. This committee found that "living in" is not necessary for all nurses, although the matron, the sisters in charge of acute wards and the nursing students should still be resident. It is suggested that for those resident the traditional nurses' home (which looks like an apartment house) is not necessary and that a ranch type or two-story building of cottage type would be more suitable. Hospital authorities are also asked to consider maintaining a register of approved lodgings for nurses and the acquisition of large houses that might be converted into flats or single rooms where the staff could make their own arrangements for catering, cooking and common services. The committee considers that "living out" gives the nurse a greater sense of independence and a closer contact with the outside world and hence a better insight into patients' problems.

The real reason that the Ministry of Health is anxious for nurses to live out is, of course, once more financial, for the cost of providing nurses' homes is high and the tradition that the nurse should live at

her hospital has become too expensive to maintain — even if it were desirable. So it seems that a change will come about, although the die-hards may protest; the medics and the nurses can now put out the flags.

* * *

Apropos of flags, one does not normally see so many flying from public buildings as in the United States. For this reason I was interested when I recently saw the American and British flags fluttering side by side on the roof of the Wellcome Research Institute in London. The reason was that two exhibitions of Anglo-American interest were being held. The first was to commemorate the centenary of the birth of Sir Henry Wellcome at Almond, Wisconsin, in August, 1853. This exhibition was to have been opened by the American Ambassador, but because he was recalled to Washington for the Foreign Ministers' meeting, his speech was read by Dr. Ralph Wyckoff, scientific attaché to the Embassy. He described Wellcome as one who scorned the modern need of specialization and recalled the great benefit that millions of people had derived from the compressed drugs that he had done so much to introduce. Scientific and practical enterprises had sprung from the success of the firm of Burroughs, Wellcome and Company, for Sir Henry had supported ambitious research projects with the firm's profits. Emphasizing this, Sir Henry Dale, O.M., F.R.S., chairman of the Wellcome Trust, said that, as long ago as 1904, Wellcome had the idea of a progressive pharmaceutical industry, based on research and scholarship far beyond its immediate needs and devoting its dividends to further research. Carrying out these principles of its founder, the Trust had already spent half a million pounds, had been able to endow two chairs in the University of London, and had made grants to medical laboratories in Australia and New Zealand and to the new pathological museum at the Royal College of Surgeons and to the Research Library at the Royal Society of Medicine. The Exhibition itself illustrated incidents in the life of Wellcome from the time of his early days in Wisconsin when his family was nearly wiped out by Sioux Indians, through his days as a pharmaceutical student and commercial traveler in the United States, right up to the time of the success of his business and the conferring of his Knighthood in 1936.

The other exhibition at the Wellcome Institute formed part of the first International Congress of Medical Librarianship and illustrated the services of the Armed Forces Medical Library at Washington. Opening this exhibition, Colonel Eissler, of the American Embassy, described how the library was founded in 1836 and how between the years 1868 and 1895, John Shaw Billings held the position of Librarian and enlarged it from 5,000 to 100,000 volumes and began the great *Index-Catalogue*, which today serves the medical world as the current list of medical literature. As president of the Congress of Librarians, Sir Cecil Wakeley had already paid tribute to the value of this index as a means of finding one's way through the labyrinth of the world's medical journals. A measure of the importance of such a guide was provided by the exhibition of the world's medical periodicals at B.M.A. House, where 2500 journals from 68 countries were on display — 1500 more were not included for lack of space. Perhaps these sobering figures should make those who use a pen pause a moment before they raise it and ask whether their writing is really necessary.

* * *

A doctor remarked to me the other day that he really thought the National Health Service had gone too far — a patient asked him to prescribe a vacuum cleaner to remove the dust from her house, since her child had asthma.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

CASE 39391

PRESENTATION OF CASE

First admission. A sixty-one-year-old merchant was admitted to the hospital because of anorexia and vomiting.

Seven months previously the patient began to notice hunger pains if he did not eat frequently. Four months later he saw a physician who prescribed Gelusil, which gave some relief. Five days before admission, anorexia became marked, and for the last three days, he had vomited almost everything taken by mouth.

Physical examination revealed a well nourished and well developed man. The only abnormal findings were a Grade 1 systolic murmur at the apex and a left hydrocele. No abdominal mass was noted.

The temperature, pulse and respirations were normal. The blood pressure was 145 systolic, 85 diastolic.

The urine had a specific gravity of 1.024 and gave a ++ test for albumin; the sediment contained 2 red cells and 15 white cells per high-power field, and was loaded with hyaline casts with an occasional granular cast. Examination of the blood disclosed a hemoglobin of 13.6 gm. per 100 cc. and a white-cell count of 11,200. The nonprotein nitrogen was 60 mg. per 100 cc. A phenolsulfonephthalein test showed 75 per cent excretion of the dye in two hours. A gastric analysis demonstrated free hydrochloric acid and a normal amount of fluid. Two stool specimens were guaiac negative.

An upper gastrointestinal series revealed diffusely prominent mucosal folds in the stomach, with hyperperistalsis but no intraluminal lesions. The duodenal bulb was extremely irritable and persistently deformed. No ulcer crater was demonstrated fluoroscopically, but the films showed a small fleck in the proximal or middle portion of the duodenal bulb to which the folds radiated. There were pronounced hypertrophic changes in the lower dorsal and upper lumbar spine.

The patient was put on a bland ulcer diet, and improved greatly. The casts disappeared from the urine, and the number of white cells in the sediment fell to 8 per high-power field. The nonprotein nitrogen fell to 30 mg. per 100 cc. The white-cell count remained over 10,000. Sigmoidoscopy to a distance of 15 cm. was negative.

The patient was discharged on the twelfth hospital day to continue on an ulcer diet with Gelusil, phenobarbital and atropine.

Second admission (six months later). After discharge the patient spent the first months at home because he felt tired and was easily fatigued. He then returned to work and felt much better. He continued to feel fairly well until a month before the second admission, when he began to notice the onset of more fatigability, weakness, anorexia and the feeling that his stomach was always filled with food. He had gained 10 pounds since his hospitalization but again began to lose weight and had lost 15 or 20 pounds. Symptoms persisted over the next two or three weeks, and his physician found the hemoglobin to be 6.3 gm. per 100 cc. Liver was prescribed, but a few days later the patient noted that his stools were black whereas previously he had never observed any change in them. The symptoms mentioned previously continued, and he also had some belching but no actual epigastric pain or indigestion. He denied nausea, vomiting or any change in bowel habit except that for the past week he had a little more tendency to be constipated. He did not have dizziness, fever or sweating but did have chilly sensations. He denied jaundice, symptoms referable to the right upper quadrant or red blood in the stool.

Physical examination disclosed a thin man who appeared chronically ill. The lungs were clear; there was a Grade 2 systolic murmur over the entire precordium. In the right upper quadrant there was a firm, nodular mass extending to the midline and to the umbilicus. The same observer believed this to be liver on one occasion and a mass involving the transverse colon, duodenum and stomach on another.

The temperature was 101°F., the pulse 96, and the respirations 20. The blood pressure was 100 systolic, 60 diastolic.

The urine had a specific gravity of 1.028 and aside from occasional white cells and a rare hyaline cast in the sediment was normal. Examination of the blood revealed a hemoglobin of 6.3 gm. per 100 cc. and a white-cell count of 20,000, with 87 per cent neutrophils. The serum sodium was 137 milliequiv., the chloride 84 milliequiv., and the potassium 3.7 milliequiv. per liter. The total protein was 5.4 gm., the albumin 3.2 gm., the globulin 2.2 gm., and the alkaline phosphatase 1.4 units per 100 cc. A cephalin-flocculation test was negative in twenty-four and + in forty-eight hours. The prothrombin time was 17 seconds (normal, 14 seconds).

Stool and vomitus were both guaiac negative on one occasion, and a stool was guaiac positive on another.

An x-ray film of the chest was unremarkable. A gastrointestinal series showed gastric distention, with complete obstruction at the pylorus (Fig. 1). There was irregularity of the distal stomach. On

FIGURE 1.

barium-enema examination, barium flowed without obstruction to a point just distal to the hepatic flexure, where it pooled in an irregular fashion (Fig. 2). There was no obstruction at this point, however, and the barium flowed on to fill the cecum and appendix. After evacuation, a good deal of barium was trapped in the irregular area in the transverse colon.

A Levin tube was passed, and several transfusions given. On the ninth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. STANLEY M. WYMAN*: My first reaction to this history was that it was a fairly typical picture of peptic ulceration with obstructive symptoms. The patient had no particularly remarkable symptoms otherwise. I shall not go into the problem of the renal picture; I am sure he had some form of kidney disease, but since presumably we shall not have that information I think it is futile to speculate. In any event, the renal disease was largely reversible.

The x-ray examination on the first entry is frustrating technically in some respects. It was reported as showing a normal esophagus. There is some prominence of mucosal folds in the stomach, but I cannot attach too much significance to that. There does seem to be some narrowing of the duodenal cap on these spot films. Other spot films show what may be a very small crater in the center of the duodenal cap. Those inconclusive findings, together with the history, which seems quite typical, impel me to a conclusion that this man had a duodenal deformity and perhaps an active crater from duodenal ulcer. I think the changes in the stomach were presumably those of gastritis associated with this. In view of the later events I looked particularly for some irregularity in the distal stomach that might point to the findings that we are going to see later, but I cannot see a filling defect in this region and no mass was reported on physical examination; therefore, I cannot go beyond calling this a simple duodenal ulcer at the moment.

FIGURE 2.

The patient went home and did something rather unusual for most patients with duodenal ulcer — he stayed home for the first months because he felt tired and became easily fatigued. Most patients with a duodenal ulcer are on the job promptly once they are put on a good regimen; most of them pick up rapidly. There is a note in the record of increas-

*Radiologist, Massachusetts General Hospital.

ing fatigability, weakness, anorexia and weight loss — the weight lost being 15 to 20 pounds. The hemoglobin was 6.3 gm.; that is distinctly unusual for an ulcer patient who is on a good regimen, and makes one wonder immediately about an intercurrent disease if not complications of the duodenal ulcer. Of course, carcinoma is the most likely condition to be considered. The stools became black, suggesting bleeding from high in the gastrointestinal tract unless I assume that the black color was due to ingested material. He was thin and appeared chronically ill on physical examination. I was given more information this morning about the mass described in the right upper quadrant. The examiner informed me that it was very hard and somewhat nodular and descended with inspiration, and that he was convinced that he could get his hand between the mass and the liver. He personally thought it was the gall bladder. Obviously, this is a perfectly good picture for neoplastic disease by clinical criteria, by physical examination and by the laboratory studies. I am not going to pay much attention to the report of the chemical studies; the serum sodium, chloride and potassium were slightly low, I am told, presumably because of prolonged vomiting.

The x-ray studies with which I am unfortunately confronted present a very unusual picture. The one good film of the gastrointestinal series shows no passage of barium beyond the pylorus, and the examiner told me that during the time that he watched this patient, he never saw any filling of the duodenal cap (Fig. 1). There is a definite suggestion of something pressing in on the lesser curvature of the stomach at this point. This suggests that this is the x-ray counterpart of the palpable mass felt in the right upper quadrant. The question is, Was it intrinsic or extrinsic? An intrinsic growth in the stomach will deform and destroy mucosal folds, will invade and will present as an intraluminal mass. I do not have evidence of such a process on these films; unfortunately I have no other films to study. I think if we had entirely adequate films of this area, we might be a good deal closer to answering that very important question. At the moment it seems as though this was an extrinsic pressure on the lesser curvature of the stomach above the pylorus — that is, in the antrum and prepyloric region.

The films show a normal distal colon, but there is an irregular pooling of barium in the proximal transverse colon (Fig. 2). This barium lies in a very irregular pool, apparently outside the colon to a great extent. There is perhaps some suggestion of nodularity in the lumen of the colon more proximally, and a suggestion of something pushing in. Here, again, I think if we had good compression spot films taken with the patient turned so that his right side was elevated, we could see this lesion better in profile and thus learn more about it. The same problem that I enumerated in the stomach is present here: Was this process intrinsic or extrinsic? I think there is some evidence that this mass had extended into the lumen of the colon and that barium had left the confines of the colon to fill this somewhat irregular pool. This is directed toward the same general region as the mass pressing on the stomach, so I should think we have to call this part and parcel of the same process.

What are the possibilities? The old duodenal ulcer may have penetrated sufficiently to form a large inflammatory mass and then may have formed an abortive sinus into the colon. Such duodenocolic fistulas have been reported, although they are quite uncommon. I do not have the evidence to call that a duodenocolic fistula; certainly, I think it would be farfetched to ascribe this to peptic ulceration. Could this have been inflammatory gall-bladder disease? It most certainly could, but again I think that would be stretching matters too far. Other inflammatory processes must be borne in mind — a foreign body could have perforated out of the colon, producing an abscess. Actinomycosis is a common cause of this sort of fistula formation, but it more frequently occurs in the cecum. That is also true of a foreign-body perforation.

By all odds the most likely explanation is neoplastic disease. I think the real problem comes in deciding where I ought to localize this process and what particular type of cancer I ought to call it. As I see it, there are geographically three main problems. Was this carcinoma of the gall bladder, stomach or colon? Gall-bladder carcinoma is the rarest of the three. Usually, it occurs in the presence of previous gall-bladder disease, and, if one is fortunate, one may see gallstones; neither of these was present here. The stomach? I see no way to exclude carcinoma of the stomach. I think if we had a better x-ray examination of the stomach, I might be able to exclude this completely. The third possibility — that of cancer of the colon — is perhaps the best. The evidence points to a definite suggestion of involvement of the colon intrinsically. There is some filling of a pocket from the colon, suggesting that its origin was in the colon. I should choose as the most likely possibility, therefore, neoplastic disease arising in the colon and invading the wall of the stomach, but not actually growing into its lumen. The patient, I think, had an old duodenal ulcer. I shall not go into all the types of neoplasm that could occur; we should bear in mind that lymphoma can produce unusual pictures with fistula formation, but I think the best bet is carcinoma.

DR. ALLEN G. BRAILEY: I should think the fact that the patient had a duodenal ulcer would argue against carcinoma of the stomach.

DR. WYMAN: Yes; that is an argument against carcinoma of the stomach; it does not ensure against carcinoma of the colon.

CLINICAL DIAGNOSES

Duodenal ulcer.
Carcinoma of colon.

DR. STANLEY M. WYMAN'S DIAGNOSES

Carcinoma of colon invading wall of stomach.
Duodenal ulcer, healed.

ANATOMICAL DIAGNOSIS

Adenocarcinoma, Grade 3, of hepatic flexure of colon, with extension to duodenum, stomach and pancreas and metastases to regional lymph nodes.

PATHOLOGICAL DISCUSSION

DR. ROBERT H. FENNELL, JR.: Dr. Linton, would you tell us the opinion on the ward.

DR. ROBERT R. LINTON: I would first like to compliment Dr. Wyman on an excellent analysis of this patient's condition, and I am glad to say that with the help of our roentgenological department we came to the same conclusion — that this patient had a huge carcinoma of the transverse colon, involving the duodenum, to produce complete pyloric obstruction. I am certain that, when we saw him on the first admission, this lesion was undoubtedly present but not nearly so large, since it could not be palpated. I was certain on the last admission that the mass was not connected with the liver since it was possible to separate it from the liver quite definitely. Since on a gastrointestinal series we found an active duodenal ulcer, we unfortunately assumed that this was the cause of the symptoms, as it may well have been at that time. It has always been my teaching, because I too have been taught it, that in doing a gastrointestinal series one should start with a barium enema and complete the examination with an upper gastrointestinal series. I am glad that this case has been presented here at this conference, if for no other reason than to re-emphasize this point. If this lesion had been picked up on the first admission there is no question that the patient would have had a better chance of cure from the lesion.

I have seen a number of patients with large carcinomas in this region that involved the duodenum, and it is impossible to remove the primary lesion without doing the so-called Whipple operation, necessitating the excision of the pylorus, duodenum and head of the pancreas. This was the operation we did, in addition to removing the ascending colon. This necessitated an end-to-end anastomosis between the body of the pancreas and the jejunum, an end-to-side anastomosis between the common bile duct and the jejunum, a gastrojejunostomy and an ileotransverse colostomy.

DR. FENNELL: When this mass was dissected, a large ulcerating carcinoma involving the hepatic flexure of the colon was found. The tumor was quite extensive, about 8 cm. in length, and had completely encircled the colon. It had extended to the stomach and had invaded the wall of the stomach and the duodenum; I am sure that is the explanation for the defect seen on the x-ray film. The tumor was an adenocarcinoma, as Dr. Wyman predicted, although in some areas it was undifferentiated. A number of lymph nodes were involved, but the lymph nodes near the resection margin were free of tumor. There was no evidence of a duodenal ulcer.

DR. LINTON: I am glad to report that this patient to date (about two months after operation) has made an extraordinarily satisfactory convalescence and was discharged home on his nineteenth postoperative day. I hope it is of significance, as far as prognosis is concerned, that the liver contained no metastases and the highest lymph nodes removed from the gastrohepatic ligament and around the hepatic artery also gave no evidence of involvement.

CASE 39392

PRESENTATION OF CASE

A fifty-one-year-old man was admitted to the hospital because of chest pain and low-grade fever.

Twelve years before admission, when the patient had pleurisy and bronchopneumonia, a roentgenogram of the chest was said to have shown a cyst in the lung. Subsequently, he was rejected by one branch of the military services but accepted by another during the recent war, and went through a hazardous and strenuous tour of duty without difficulty. Two years before admission a routine x-ray film of the chest disclosed a cyst in the right upper-lung field. For the eight months before admission the patient was asymptomatic except for a feeling of extreme tiredness at the end of the day's work. He was not aware of having fever during this period. Three weeks before admission he had mild chest pain and fever starting with a mild sore throat and generalized malaise. After a week of bed rest, the chest pain, which was limited to the right upper part of the chest and present only on coughing, subsided completely; however, he was left with a low-grade fever (maximum temperature of 100°F.) and a feeling of extreme exhaustion and apathy.

He had had a chronic cough, which he attributed to smoking two packages of cigarettes daily, and he coughed up about a tablespoonful of sputum daily. He had never had hemoptyses, chills or sweats, and he had gained 3 pounds in the last three months.

Physical examination revealed a middle-aged man in no distress. The heart was not remarkable. Tactile fremitus was reduced over the right upper aspect of the chest posteriorly, and there were

diminished breath sounds in the same area. Otherwise, the lungs were clear to percussion and auscultation. The left supraclavicular lymph node, palpable between the heads of the sternocleidomastoid muscle, was enlarged, soft and freely movable. The remainder of the physical examination was not remarkable.

The temperature was 99°F., the pulse 88, and the respirations 20. The blood pressure was 120 systolic, 80 diastolic.

The urine was normal. The hemoglobin was 14.4 gm. per 100 cc., and the white-cell count 12,100, with 84 per cent neutrophils, 15 per cent lymphocytes and 1 per cent monocytes. An electrocardiogram was within normal limits. A chest film revealed in the right apex a smooth-lined cyst measuring 11 cm. in length by 9 cm. in width containing air and fluid (Fig. 1). There was atelectasis and possibly pneumonitis of the lung adjacent to the cyst. The left apex showed a few linear scars; otherwise, the lung fields were clear. The esophagus was displaced slightly to the left, but showed no intrinsic abnormality. The heart shadow was within normal limits.

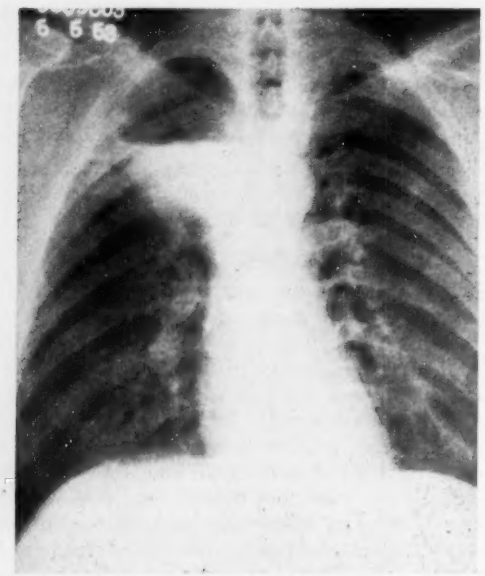

FIGURE 1. *Roentgenogram of the Chest.*
Note the thin-walled cavity with a fluid level at the right apex.

On the third hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. WILLIAM R. WADDELL*: This case appears to be relatively simple. The diagnosis is suggested in the description of the patient's history and the more detailed description of the roentgenograms of the chest. Cystic conditions in the lung are most readily diagnosed by aid of the roentgenograms, but even with that diagnostic tool, the different types of cysts are often not very accurately differentiated. I think it would be worth while to look at the x-ray films.

DR. JOSEPH HANELIN: A large thin-walled cystic cavity, approximately 10 cm. in greatest dimension, is present at the right apex with a fluid level across its midportion (Fig. 1). I do not see anything projecting from the cyst wall into the lumen of the cyst. Below this cavity there is some irregular streaking in the lung, and in the left subapical region there are irregular densities consistent with old scars. The cyst is also seen in the spot film; the upper esophagus is displaced somewhat toward the left side. The heart itself seems quite normal.

DR. WADDELL: Actually, no pulmonary tissue can be seen completely surrounding the cyst; it is only on the inferior aspect of the cystic mass.

DR. HANELIN: The cyst comes up to the apex of the thorax as far as I can tell. No lateral film is available.

DR. WADDELL: I do not think a lateral view would contribute much to the definition of the lesion; the mass lies in the apex.

Cystic conditions involving the chest may have a number of different origins. This history is characteristic of infection occurring in a cyst known to have been present for many years — at least twelve years. Presumably, for the majority of the twelve years the patient had no difficulty from the cyst and needed attention only with the onset of infection. Tumors arising within the lung and within the mediastinum can become cystic, usually by necrosis of the central portion. The necrotic material is sometimes evacuated through an open bronchus, and the final x-ray appearance, like the appearance that was present in this patient on admission, may be that of a cyst. Tumors that degenerate and leave cystic masses, however, usually show a fairly thick wall and irregularity of the lining that are suggestive if not diagnostic. The smooth character of the cyst wall inclines me to eliminate tumors — bronchogenic tumor, lymphomatous masses and neoplasms such as teratomas — from serious consideration. The finding of a palpable lymph node in the left supraclavicular area might lead one to consider that diagnosis somewhat more seriously, but the description of its physical characteristics — namely, the softness and the ease with which it moved — probably means that it was not involved by neoplastic tissue.

There has been some discussion in the past of neoplasia arising in cysts of long duration such as congenital cysts of the pulmonary parenchyma, but that is an unusual situation and I doubt if I should be able to make such a diagnosis on the present evidence.

*Assistant in surgery, Massachusetts General Hospital.

Infectious processes can occasionally lead to the formation of cystic areas within the lung; an old burned-out lung abscess — that is, one that has practically healed — may leave a cystic cavity with an appearance much as this had. Occasionally, bronchiectasis results in cyst formation; the usual mechanism is an acute excavating infection with healing and development of an epithelial lining. With the possible exception of the episode many years previously there is nothing much to suggest infection as the etiology of this cystic mass. Occasionally, tuberculosis can cavitate, with rapid or gradual expansion of the cystic cavity; that might be further suggested by the appearance of the calcified scars in the apex of the left upper lobe. However, it seems unlikely that the patient was suffering from cavitary pulmonary tuberculosis of twelve years' duration at the time of admission, and I should put that low on the list. A pneumatocele distal to an acute inflammatory condition of the bronchi occurs occasionally, especially in children. That ordinarily does not persist for twelve years and, I think, can be dismissed without further discussion. Empyema, another inflammatory condition that could possibly account for these findings, needs consideration. I do not know how to rule that diagnosis in or out with certainty, especially since there was no lung tissue surrounding the entire cyst.

I am inclined to consider the congenital cysts of the pulmonary parenchyma and mediastinum in trying to define the etiology of this mass. These cysts can arise in the pulmonary tissue itself, in the mediastinum, in the pleura or in the pericardium, and it may be impossible in many cases even at operation to discover the exact origin of some of these masses. They are believed to arise from bits of primitive embryonic tissue that become separated from the remainder of the lung. Another condition that has received some attention lately is interlobar sequestration of the lung in which the separated pulmonary tissue either retains or picks up a blood supply from the systemic circulation. The reported cases, with one exception, have occurred in the lower lobe, the anomalous blood supply coming from the lower thoracic or upper abdominal aorta. Usually, those masses are not cystic but solid masses of sequestrated lung tissue.

Dermoid cyst is another possibility that could well explain the findings; this is one diagnosis that might have been helped if a lateral film had been available because dermoid cysts arise predominantly in the anterior mediastinum. The absence of calcification in the wall of this cyst is evidence that that is not the correct diagnosis. Occasionally, a mass of this sort arises in the esophagus as a large diverticulum.

Having considered these possibilities, my best suggestion is a congenital pulmonary cyst arising in pulmonary tissue, with secondary infection.

DR. BENJAMIN CASTLEMAN: When you speak of congenital cysts of the lung do you include the bronchogenic cysts?

DR. WADDELL: That is what I had in mind.

DR. CASTLEMAN: You would expect the cyst to be lined with bronchial epithelium.

DR. WADDELL: Yes, as well as cartilage and sometimes smooth muscle — elements that make up the bronchus. I am not certain that that is valid at all times because we have all seen unusual metaplasia, the growth of epithelium, and even the presence of cartilage, in cysts that have had an obvious infectious origin. I say that on the basis of having seen some of these specimens and having done some work on the embryology of the lung in which it was evident that the pulmonary parenchyma is really a totipotent tissue*; in other words, the same elements that can give rise to epithelial structures can also give rise to the structures that have always been considered as mesodermal — cartilage, muscle and so forth. It would not surprise me if the histologic diagnosis was inconclusive as far as the origin of the cyst was concerned. Pathologists are frequently at odds with the surgeons about the origins of those cysts.

DR. CASTLEMAN: This patient was seen on the outside by Dr. Zetzel. Perhaps he will tell us about the preoperative findings.

DR. LOUIS ZETZEL: For the eight months before admission this man had been noted by his friends to be excessively tired. He seemed perfectly well otherwise and had gained weight. When I first saw him he had nothing but the complaint of a sore throat, general malaise and pain over the right aspect of the chest on coughing. On obtaining the history of the cyst, I checked upon his previous hospitalizations. About twelve years before admission he was treated in another hospital for bronchopneumonia; an incidental finding on the chest roentgenogram was a cyst, which was described then as being in the left apex not in the right apex as we see here. Unfortunately, those x-ray films are not available. Later, when he wanted to enlist in the Army, he was turned down because of the finding of the cyst. He then consulted a chest specialist, who had further x-ray films done. Those films also are not available, but the report indicated that the cyst again was found in the left apex; no mention was made of a cyst in the right apex. This physician considered the patient to have a nonprogressive disease that would not interfere with his activities, but the Army refused to accept him. He was accepted in the Navy because no x-ray films of the chest were taken. He completed an arduous and extensive tour of duty and did well until the present acute episode. On examination he had only diminished breath sounds over the right apex. I repeated the x-ray films and noted

*Waddell, W. R. Organoid differentiation of fetal lung: histologic study of differentiation of mammalian fetal lung in utero and in transplants. *Arch. Path.* 47:228-247, 1949

the fluid; Dr. Edward D. Churchill saw him at this time and believed we were dealing with an infected cyst and that while the cyst remained, the man would continue to have the low-grade fever and extreme apathy.

Clinical Diagnosis

Infected congenital cyst of lung, right upper lobe.

Dr. William R. Waddell's Diagnosis

Infected bronchogenic cyst of lung, right upper lobe.

Anatomical Diagnosis

Pulmonary tuberculosis, with cystic cavitation.

Pathological Discussion

Dr. Castleman: Dr. Churchill removed the right upper lobe with the large cystic mass in the apex. He had to remove the parietal pleura along with the lesion which was very adherent to it at the apex; in addition, the cyst was so tense that it had to be drained with a needle before removal. In some areas the cyst merged with the lung tissue; in others there was a sharp separation between the lung and the cyst. When I opened the cyst I found a large amount of fibrinous material lining the cyst. There were yellowish-white caseous areas in the lung parenchyma that merged with the cyst.

Microscopical examination of the cyst wall showed that the grossly observed fibrinous material attached to the inner lining as well as the lining itself was active tuberculous granulation tissue. This was true not only of the cyst wall that merged with the lung parenchyma but also of the lining of the top part of the cavity that was not connected with the lung tissue. The lung tissue showed obvious active tuberculosis, and we were able to find a communication between it and the large cyst. Many sections through various parts of the cyst wall showed tuberculosis in every one of them. The regional lymph nodes were involved with active tuberculosis. We were able to find the organisms in any number of areas.

The question arose whether this was a nontuberculous cyst into which tuberculosis had spread or whether it was a tuberculous cavity originally. I favor the latter point of view. We do not see much tuberculosis in this hospital, but physicians who have seen a great deal of tuberculosis inform me that a tuberculous cavity of this size may remain in the lung for years and occasionally flares up.

Dr. Zetzel: Sputum specimens were collected before operation; direct smears were all negative. The culture and guinea-pig inoculation were not reported as positive until the patient had successfully completed convalescence after the operation.

Dr. Waddell: I should like to know what happened to the cyst on the left. If that is an accurate description, it is interesting that it went away. The patient apparently is quite well now.

Dr. Castleman: We do not know anything about that. The patient is well now, about two months after the operation.

Dr. Farahe Maloof: Did he have a total upper lobectomy?

Dr. Castleman: Yes; the middle and lower lobes were easily inflated after the removal of the upper lobe and remained inflated.

Dr. Waddell: I assume that the good health for the twelve years means he had a good communication between the cyst and the bronchial tree.

Dr. Castleman: There was a communication at the time it was removed, and I should suppose it was draining.

A Physician: Did any members of the family have tuberculosis?

Dr. Zetzel: No; the whole family had chest films that were completely normal.

Dr. Lewis Kane: It is unusual to have the wall of cysts this thin in tuberculous cavities.

Dr. Castleman: It was not too thin; in fact, it was fairly thick, even on the free surface. Of course it was fused with the parietal pleura.

Dr. Pittman, have you any comment?

Dr. Helen S. Pittman: I was sure it was a congenital cyst. We see this kind of tuberculosis so seldom that we have forgotten what it looks like. Patients used to be seen in the sanatoriums in comparatively good health with large tuberculous cavities, but I have not seen one for twenty-five years.

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NEW CONGRESSIONAL FUNCTION?

IT may have seemed curious to many who were catching up on the news recently to hear over their radios or read in their newspapers that the Senate voted to change the name of Aureomycin to the chemically more descriptive name "chlortetracycline." The passage of this bit of legislation occurred during the final spurt of activities that characterized the closing days of the last session of Congress. To those not acquainted with the facts and circumstances, this action suggested that the Congress had undertaken some new function, or perhaps that it was delving into details that it could well delegate to established administrative agencies better equipped for the purpose. Here are some of the facts that led to this action of Congress.

With the advent of penicillin during World War II, the pharmaceutical industry was introduced to a group of products that were quite different from anything it had previously handled. Since the Government was subsidizing the production of penicillin to a great extent, and since all the penicillin products were going to the armed forces, it established rigid standards for potency, stability, sterility, freedom from pyrogens and toxic substances and methods of testing to ensure that this penicillin always maintained a high degree of purity and potency. When supplies appeared to be sufficient to permit distribution to the public, the Government, in conjunction with industry, set up a system of predistribution testing before the sale of each batch. Since the Federal Food, Drug and Cosmetic Act of 1938 contained no provision to cover such testing, it was necessary to request Congress to amend the existing law to provide for a system of certification for penicillin.

Such an amendment was passed in July, 1945; it directed the administrator of the Federal Security Agency to provide for certification of drugs composed wholly or partly of any type of penicillin. The law also authorized him to set up standards of identity, strength, quality and purity necessary to ensure both safety and efficacy. The law also prohibited the distribution of penicillin-containing drugs in interstate commerce unless the penicillin was from a certified batch. A further amendment was made in March, 1947, to include streptomycin, and in July, 1949, the law was again amended to include Aureomycin, bacitracin and chloramphenicol. Aureomycin was made available commercially in December, 1948, and chloramphenicol early in 1949.

Certification as required under this law is neither necessary nor practical for drugs in general, but the important antibiotics possess peculiar and unusual characteristics. Among the characteristics of antibiotics that make certification a useful and valuable procedure in safeguarding the public health are the following: they have marked therapeutic value in one or more diseases that are major public-health problems; there are numerous possibilities of contamination or adulteration unless they are manufactured under strict controls; they are

generally unstable, and under various circumstances decomposition may occur, causing reactions or loss of potency; there may be marked variation in efficacy when the vehicle or route of administration is changed; and biologic or other methods of testing and assay are required, and these are usually less precise than chemical methods.

The primary reasons for applying the certification procedure, therefore, are the importance of the drug in combating serious and crippling diseases, and the difficulty in evaluating the final commercial material. Certification, however, does not relieve the producer of his responsibility, but emphasizes the vagaries of the drug and the need for a stringent internal control system.

None of the antibiotics made available commercially since July, 1949, have been included under the section of the law that requires certification. Such inclusion, however, is not compulsory, and, indeed, the initiative must be taken by the producer. The manufacturers of the more recent products have chosen instead to market their antibiotics as "new drugs" under the provisions of Section 505 of the Federal Food, Drug and Cosmetic Act; this requires them only to show that their products are safe when used according to the directions given for their use. Certification of individual batches is not required under this procedure.

Among the antibiotics marketed under Section 505 are Terramycin, which was made available in March, 1950, and erythromycin and carbomycin, which were released for sale during the past year. This difference in procedure explains why congressional action was not required for the adoption of the generic name oxytetracycline for Terramycin whereas the corresponding change from Aureomycin to chlortetracycline required such an action.*

At the time of its discovery, "Aureomycin" was used as the generic name for this new antibiotic because it had been derived from *Streptomyces aureofaciens*, which produces a substance with a golden color. The chemical structure of the antibiotic was unknown, but as soon as the chemists could characterize it with certainty, it became possible to give it a generic name more truly reflecting its chemical structure. Thus, the name, "chlortetracycline" was derived, and it is being put into use. However, the section of the law that provides for certification of Aureomycin uses the term "Aureomycin" as the generic name. Lederle, being the only manufacturer of Aureomycin in this country, has seen fit to declare the word "Aureomycin" as its trade name, and to use the chemically descriptive name "chlortetracycline" as the generic name. This will provide protection for products marketed by Lederle in foreign countries where trade-mark laws are extremely weak or nonexistent.

To make this change possible legally, it became necessary to have the existing law amended by Congress to incorporate the word "chlortetracycline" into section 507 of the Act, and abandon the use of "Aureomycin" throughout the law and the regulations. This amendment, which has now been enacted, will require Lederle to change its labeling as rapidly as possible to designate the word "Aureomycin" as the trade-mark, and to describe that trade-mark by the generic name "chlortetracycline." The use of the word "Aureomycin" as its trade-mark will protect the manufacturer's interest in the drug without adding additional terminology to the physicians' vocabulary.

The lack of uniformity in the law as now applied to different antibiotics clearly indicates that it should be revised and its provisions and applications made more equable. If the provision for certification serves to protect the public health and welfare, the law should be rewritten so as to make the requirements for certification automatic for all new antibiotics. However, the cumbersome provision of the law requiring an act of Congress to admit a new antibiotic under the certification requirement should obviously be changed at the same time. Authority to carry out this function could reasonably be delegated, along with other detailed procedures, to the administrative agency already charged with the duty of certifying the different batches of antibiotics under the existing law.

*Editorial. New generic names for antibiotics. *New Eng. J. Med.* 249:503, 1953.

MENTAL HEALTH IN AMERICA

CONNECTICUT, according to Dr. Jules V. Coleman, associate clinical professor of psychiatry at Yale University School of Medicine, has in its three state hospitals for mental disease "among the few really good systems in the country." Even the present superiority enjoyed by Connecticut could be improved, however, Dr. Coleman stated in a Yale broadcast, by the passage of legislation now pending that calls for the establishment in Connecticut of a state department of mental health.

Dr. Coleman's views were expanded to include the nation, and he even ventured the belief that Americans are no worse off mentally than the citizens of any other country. Such a welcome situation, so opposed to the views held by many Americans and others, apparently exists despite the preoccupation of Americans with their emotional troubles; it is a sign that Americans, having so little else to worry about, are worrying about themselves; like the dog that needs a few fleas to take his mind off his real troubles, they need a few real troubles to take their minds off their imaginary ones.

Improvement in the care of the mentally ill and the emotionally disturbed is making steady progress, as psychiatry is considered more and more to be a basic science as well as a clinical branch of medicine. Statistics-wise, although there are still only half enough psychiatrists to do the job that would be cut out for them if twice as many existed, the membership of the American Psychiatric Association rose from 2913 in 1942 to 7472 in 1952.

The story is different so far as nursing care is concerned. With half the hospital beds in the country occupied by psychiatric patients only 3 per cent of the nurses registered in hospitals are working in mental institutions. Such a marked disproportion is probably offset by a lower concentration of nursing care required in the hospitals for mental disease.

ON THE FUNCTION OF DOING NOTHING

A CONSIDERABLE degree of veneration has become attached to the memory of that retired toiler of the sea; who, when asked how he passed his time replied that sometimes he sat and thought, and sometimes he simply sat. Any person, indeed, may be said to have achieved a new and high level of maturity when, having nothing to do, he does exactly that — no more and presumably no less. For whereas sleep it is a gentle thing, beloved from pole to pole, so total idleness, with the added savor of retained consciousness, such as it is, must reach at least an equally desirable plane.

It has been suspected that the human mind is never, or almost never, completely lacking some vestigial degree of activity, at least during the life of the individual. Even when it seems at its most torpid level it is credited with turning over at the minimum number of revolutions per hour necessary to maintain some sort of intellectual steerage way. It may otherwise be compared with the hibernating groundhog, which retains still enough breath in its body to fog a very small area of a highly polished mirror ever so slightly.

Idleness, once the habit is acquired, seems to carry with it its own reward, although its pleasures may be enhanced by a contemplation of the activities of others. This does not necessarily apply to the useful work of others, for they may be watched at play and at rest as well. Inanimate objects, too, may provide their measure of entertainment, as stars move silently across the skies to the delight of celestial watchers.

The need for peaceful observation of others' efforts is well recognized by the more philosophic and kindly disposed contractors who cut peepholes in the hoardings around their excavations and sometimes provide seats at a height appropriate to the most effective use of these Judas windows.

It must be re-emphasized, however, that it is not necessarily work that requires to be watched, but all the immutable and mutable processes of nature. It is why there are bird watchers as well as steam-shovel observers and stargazers; and who today knows what may have been passing through Newton's mind, or what he may have been watching immediately prior to the episode with the apple? And who knows what impelled Henri Fabre, the gentle schoolmaster, to watch the insects in his garden, and become one of the world's great naturalists?

Actually, the mind that is capable of any constructive thought at all performs some of its most

spectacular feats when it is apparently idle — when it is daydreaming and at ease, or seems to be registering only what the eyes take in as they watch the motions of the hands in the performance of some physical task. It is why, for brain workers, there are fat dividends in the relaxation that comes from recreation, from hobbies and from pure idleness.

MURINE EOSINOPENIA

MICE, according to investigators in the realm of zoology at the University of Wisconsin, experience a lowering of the blood eosinophil count when maintained under conditions of continued cold. The thermal stress increases the activity of the adrenal cortex, with a resultant effect on the red-staining polymorphonuclear leukocytes.

Harvard scientists, the University of Wisconsin News Service also reports, have engaged in a similar, somewhat more complex study on the higher primates. Athletes just before important games — as well as their coaches — suffer such a degree of emotional strain that their eosinophil count is likewise depressed.

The Wisconsin scientists, working at fever pitch, have found that both cold and warm mice have a diurnal rhythm in the eosinophil count, which rises during the day and sinks under the stress of the well known night life of *Mus musculus*. Human beings, contrariwise, have certain tides in the affairs of men that increase their eosinophil counts at night and depress them in the daytime. Perhaps a simple differential blood count will be employed as the final, authoritative answer to the oft-recurring question, "Are we mice or are we men?"

Medical Companion and Temperance Advocate. — *at Yazoo City, Mississippi, a monthly periodical is published with the above title. It may be considered a worthy "medical companion" by those who have never seen anything superior.*

Boston M. & S. J., *September 28, 1853*

MASSACHUSETTS MEDICAL SOCIETY

DEATH

CANAVAN — Myrtelle M. Canavan, M.D., of Boston, died on August 26. She was in her seventy-fifth year.

Dr. Canavan received her degree from Woman's Medical College of Pennsylvania in 1905. She was formerly curator of the Warren Anatomical Museum, Harvard Medical School, and assistant pathologist at Boston State Hospital, and was a member of the International Association of Medical Museums, Norfolk District Medical Society Association for Research in Nervous and Mental Diseases, New England Society of Psychiatry, Massachusetts Psychiatric Society and New England Pathological Society, secretary-treasurer of the Massachusetts Medico-Legal Society and a fellow of the American College of Physicians, and the College of American Pathologists.

Dr. Canavan is survived by a nephew.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR AUGUST, 1953

RÉSUMÉ

DISEASE	AUGUST 1953	AUGUST 1952	SEVEN-YEAR MEDIAN
Chancroid	3	0	0
Chicken pox	116	100	179
Diphtheria	4	0	17
Dog bite	1054	1196	1196
Dysentery, bacillary	92	5	5
Encephalitis, infectious	2	4	0
German measles	56	151	63
Gonorrhea	266	181	260
Granuloma inguinale	0	0	0
Hepatitis, infectious	53	38	8†
Lymphogranuloma venereum	3	0	1
Malaria	0	25	1
Measles	41	103	317
Meningitis, meningococcal	2	4	4
Meningitis, Pfeiffer bacillus	0	4	2
Meningitis, pneumococcal	0	0	0
Meningitis, staphylococcal	0	0	0
Meningitis, streptococcal	1	1	0
Meningitis, undetermined	2	2	4
Mumps	342	153	268
Poliomyelitis	114	192	94
Salmonellosis	28	11	12
Scarlet fever	55*	40	66
Syphilis	200	156	166
Trichinosis	3	3	3
Tuberculosis, pulmonary	149	153	186
Tuberculosis, other forms	10	10	13
Typhoid fever	1	4	4
Undulant fever	0	1	2
Whooping cough	166	108	379

*Includes streptococcal sore throat.

†Four-year median.

COMMENT

Diseases below the seven-year median were chicken pox, diphtheria, measles, scarlet fever and whooping cough.

There were four cases of diphtheria reported for the month of August, which brings the total for the year to 21, a remarkably low figure.

The 41 reported cases of measles make this the lowest figure by far for the month of August in the history of this state.

Diseases above the seven-year median were bacillary dysentery, infectious hepatitis, mumps and salmonellosis.

The number of cases of bacillary dysentery (92) reported for August was the same as that reported in July, and before that time, the highest since December, 1943. Boston and Worcester

have been experiencing sharp outbreaks during this period. Person-to-person contact appeared to be the principal avenue of spread.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

The following diseases were reported from the communities named:

Diphtheria: Boston, 3; Somerset, 1; total, 4.

Dysentery, bacillary: Belmont, 3; Boston, 39; Brockton, 4; Brookfield, 1; Cambridge, 1; Danvers, 9; Greenfield, 1; Lawrence, 1; Lowell, 1; Lynn, 3; Marblehead, 1; Medford, 1; Methuen, 1; Somerville, 1; Springfield, 2; Worcester, 22; Wrentham, 1; total, 92.

Encephalitis, infectious: Attleboro, 1; Greenfield, 1; total, 2.

Hepatitis, infectious: Attleboro, 1; Auburn, 1; Boston, 11; Brockton, 1; Cambridge, 3; Chelsea, 1; Dedham, 1; Everett, 1; Fall River, 1; Falmouth, 1; Fitchburg, 3; Holyoke, 1; Leicester, 1; Lynn, 3; Millbury, 8; Milford, 1; Northboro, 1; Palmer, 1; Shrewsbury, 1; Springfield, 3; Ware, 1; Westboro, 1; Worcester, 5; Wrentham, 1; total, 53.

Lymphocytic choriomeningitis: Adams, 2; total, 2.

Meningitis, meningococcal: Fall River, 1; Worcester, 1; total, 2.

Meningitis, streptococcal: Falmouth, 1.

Meningitis, undetermined: Fall River, 2; total, 2.

Poliomyelitis: Arlington, 1; Ashburnham, 1; Beverly, 4; Boston, 2; Brockton, 1; Brookline, 2; Chelmsford, 1; Chelsea, 1; Chicopee, 2; Cohasset, 2; Danvers, 2; Duxbury, 3; Easton, 1; Fall River, 3; Falmouth, 5; Framingham, 2; Grafton, 1; Great Barrington, 1; Hanover, 1; Hardwick, 1; Haverhill, 2; Holyoke, 4; Hull, 5; Huntington, 2; Leominster, 1; Lynn, 2; Malden, 1; Mansfield, 1; Marblehead, 1; Medford, 1; Melrose, 2; Middleboro, 1; Murphy Army Hospital, 1; Natick, 3; New Bedford, 3; Newton, 6; North Andover, 1; North Reading, 1; Norton, 1; Norwell, 1; Palmer, 2; Pittsfield, 2; Quincy, 3; Rockport, 1; Salem, 2; Somerville, 1; South Hadley, 1; Springfield, 9; Taunton, 1; Wakefield, 1; Waltham, 2; Watertown, 2; Wellesley, 2; West Springfield, 1; Weston, 1; Worcester, 5; Yarmouth, 1; total, 114.

Salmonellosis: Arlington, 1; Attleboro, 1; Boston, 4; Grafton, 13; Holyoke, 2; Lawrence, 1; Ludlow, 1; Lynn, 1; Malden, 1; Salem, 1; Springfield, 1; Worcester, 1; total, 28.

Trichinosis: Lawrence, 1; Marion, 1; North Andover, 1; total, 3.

Typhoid fever: Revere, 1.

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS

The October schedule of the Consultation Clinics for Crippled Children in Massachusetts is as follows:

ORTHOPEDIC CLINICS	DATE	CLINIC CONSULTANT
Greenfield	October 1	Charles L. Sturdevant, M.D.
Salem	October 5	Paul W. Hugenberger, M.D.
Gardner	October 6	Carter R. Rowe, M.D.
Haverhill	October 7	William T. Green, M.D.
Brockton	October 8	George W. Van Gorder, M.D.
Lowell	October 9	Albert H. Brewster, M.D.
Worcester	October 16	John W. O'Meara, M.D.
Lynn*	October 19	Daniel M. Killoran, M.D., and John J. Crowley, M.D.
Springfield	October 20	James D. Fisher, M.D.
Pittsfield	October 21	Edward J. Coughlin, Jr., M.D.
Hyannis	October 22	Paul L. Norton, M.D.
Fall River	October 26	David S. Grice, M.D.

RHEUMATIC-FEVER CLINIC	DATES
North Reading	October 6, 13, 20, 27
Fitchburg	October 7, 14, 21, 28

PLASTIC CLINIC	HELD	CONSULTANT
Eastern Massachusetts	Semi-monthly	Bradford Cannon, M.D.
Western Massachusetts	Monthly	Joseph M. Baker, M.D.

Physicians referring new patients to clinic should get in touch with the district health officer to make appointments. Patients are seen by appointment only.

*This clinic serves Lynn, Lynnfield, Saugus, Nahant, Revere, Chelsea, Everett and Winthrop. Referrals should be made directly to the Lynn Hospital.

BOOK REVIEWS

Appraising Personality: The use of psychological tests in the practice of medicine. By Molly Harrower, Ph.D. 8°, cloth, 197 pp., with 19 illustrations and 17 charts. New York: W. W. Norton and Company, 1952. $4.00.

Molly Harrower is well known for her research experiences in psychologic testing and her practical familiarity with a large battery of psychologic tests. This volume brings together her material and presents it for the use of physicians in view of the increasing interest general practitioners have shown. Her concluding remarks and suggested readings are practical and provocative. The book is interesting and up to date.

MERRILL MOORE, M.D.

Experimental Diagnostics of Drives. By Dr. Med. L. Szondi. Translated by Gertrude Aull. 4°, cloth, 220 pp., with 66 illustrations and 48 tables. New York: Grune and Stratton, 1952. $13.50.

Drives, sometimes called instincts, impulses or needs, appear to be the motor or engine in the human machine. The way they are distributed is illustrated by behavior directed toward conscious or unconscious goals. This is the most scholarly volume on this complicated subject that has appeared to date. The material has been approached objectively and is well organized, and the presentation is extremely interesting. It will give psychiatrists, as well as physicians, an opportunity to consider the meaning of many common terms used verbally in descriptive analysis of human behavior.

MERRILL MOORE, M.D.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

How to Have a Happy Child. By Beulah France, R.N. With an introduction by Milton Levine, M.D. 12°, cloth, 130 pp. New York: Sterling Publishing Company, Incorporated, 1952. $2.50.

This small book deals, in common-sense language, with the care and management of the young child. A bibliography is appended to the text, and a good index is provided.

Bedside Diagnosis. By Charles Seward, M.D., F.R.C.P. (Edin.), consulting physician, Princess Elizabeth Orthopoedic Hospital, West of England Eye Infirmary and the Ministry of Pensions, and Honeyman Gillespie Lecturer. With a foreword by Sir Henry Cohen, M.D., F.R.C.P., professor of medicine, University of Liverpool. Second edition. 12°, cloth, 380 pp., with illustrations. Edinburgh: E. and S. Livingstone, Limited, 1952. $3.50.

This second edition of a standard manual has been revised and brought up to date. The subject material has been arranged by symptoms, beginning with pain and ending with pyrexia. There is a good index, and the small book is well published.

NONCLINICAL NOTES

ESTABLISHMENT OF BERYLLIUM CASE REGISTRY

A man-made illness of considerable interest has been reported in the medical literature in this country since 1943 under various titles, in general referring to its association with exposure to certain beryllium compounds. As the years go by, more cases continue to appear from a variety of industrial and research operations using beryllium compounds. With funds supplied by the Atomic Energy Commission, it is planned to develop a beryllium case registry at the Massachusetts General Hospital. The purpose is to enable a study of the epidemiology of this disease, an evaluation of the beryllium hazard of incriminated operations, and dissemination of knowledge of the clinical course of beryllium poisoning, especially in relation to its medical management. The material collected is to be available for study,

and from time to time data will be sent to participating physicians summarizing facts that have been established.

This description is presented in the hope that physicians, roentgenologists and pathologists who have knowledge of cases of beryllium poisoning will participate in making the beryllium case registry complete. Facilities and funds are available for prompt handling of any material submitted, such as case records, x-ray films and tissue. It is planned to keep cases entered in the registry anonymous.

Any correspondence will be welcome.

NOTICES

ANNOUNCEMENT

Dr. Hyman Alford announces the removal of his office to 910 Commonwealth Avenue, Newton Center, for the practice of pediatrics.

EDWARD K. DUNHAM LECTURES

Wilhelm S. Feldberg, M.D., F.R.S., head of the Physiology and Pharmacology Laboratory, National Institute for Medical Research, London, will deliver three lectures in the amphitheater of Building D, Harvard Medical School, at 5 p.m., on the general subject "The Autonomic Nervous System and Chemical Transmission of Nerve Effects." The dates and subjects of the lectures are as follows:

Monday, October 5. The Physiology of the Autonomic Nervous System.
Wednesday, October 7. Chemical Transmission of Nerve Effects.
Friday, October 9. Special Problems of Chemical Transmission of Nerve Effects.

PROFESSIONAL EDUCATION COLOR TELEVISION BROADCASTS

The American Cancer Society, in conjunction with the facilities of the Columbia Broadcasting System TV Network, will produce during 1953–54 a series of closed-circuit color television programs for doctors in general practice.

A series of thirty, one-hour closed-circuit color television broadcasts, which can be viewed by practitioners in six major cities in the northeast (Boston, Philadelphia, Pittsburgh, Detroit Toledo and New York), will begin on Wednesday, October 21, 5 to 6 p.m., from a studio in Frances Delafield Hospital at Columbia University. Programs will be broadcast on alternate Wednesdays up to December 2, after which they will be presented weekly. It is hoped that this program will be extended to other cities as the series progresses.

The programs will be color kinescoped, and the Kinescopes will ultimately be made available to local medical societies through regional and state offices of the American Cancer Society.

MASSACHUSETTS SOCIETY OF EXAMINING PHYSICIANS

The fall meeting of the Massachusetts Society of Examining Physicians will be held at the Harvard Club, Boston, on Wednesday, November 18, at 6:30 p.m. After the dinner Dr. Paul Hawley, of Chicago, director of the American College of Surgeons, will speak on the subject "Some of the Present-Day Problems as They Affect the Profession, the Individual Doctor and the Public." All interested physicians are cordially invited to attend.

NEW ENGLAND CARDIOVASCULAR SOCIETY

A special meeting of the New England Cardiovascular Society will be held on Wednesday, October 14, at 8 p.m., in Morse Auditorium, Museum of Science, Boston. Dr. Paul Wood, director, Institute of Cardiology, London, England, will speak on the subject "Remarks of Current Interest on Congenital Heart Disease." Physicians, medical students and members of the New England Postgraduate Assembly are cordially invited to attend.

GRANTS IN CANCER RESEARCH

The Committee on Growth of the National Research Council, acting for the American Cancer Society, is accepting applications for grants for scholars in cancer research until January 1, 1954. The awards are designed to cover the interval between the completion of fellowship training and demonstration of competence as an independent investigator. A grant of $18,000, payable over three years, will be made to each scholar's institution as a contribution to his support and research. Each institution may submit more than one application. The grants are not restricted to the support of persons who have held American Cancer Society Fellowships. Further information may be obtained from the Executive Secretary, Committee on Growth, National Research Council, 2101 Constitution Avenue, N. W., Washington 25, D. C.

INTERNATIONAL SYMPOSIUM ON VIRUS INFECTIONS

An international symposium on the dynamics of virus infection will be held at the Henry Ford Hospital, Detroit, Michigan, October 21 through 23. The moderators for the sessions will be Drs. Thomas M. Rivers, New York, John G. Kidd, New York, Albert E. Sabin, Cincinnati, John Paul, New Haven, A. J. Rhodes, Toronto, and Gilbert Dalldorf, Albany. All interested physicians are cordially invited to attend. Further information may be obtained from Dr. Edward L. Quinn, Secretary, International Symposium on Virus Infections, Henry Ford Hospital, Detroit 2, Michigan.

SOCIETY MEETINGS AND CONFERENCES

SEPTEMBER 30. Essex North District Medical Society. Page 470, issue of September 10.
OCTOBER 2. Phi Delta Annual Lecture. Page 470, issue of September 10.
OCTOBER 4–9. American Academy of Pediatrics. Page 1126, issue of June 25.
OCTOBER 5, 7 AND 9. Edward K. Dunham Lectures. Notice above.
OCTOBER 5–DECEMBER 7. Postgraduate Seminar in Neurology and Psychiatry. Page 428, issue of September 3.
OCTOBER 5–DECEMBER 21. Hartford Medical Society Program. Page 260, issue of August 6.
OCTOBER 7–DECEMBER 2. Course in child psychiatry (pediatric neuropsychiatry). Page 428, issue of September 3.
OCTOBER 8. New York Diabetic Association. Page 470, issue of September 10.
OCTOBER 12–14. National Gastroenterological Association. Page 260, issue of August 6.
OCTOBER 12–14. Medical and Dental Military Symposium. Page 470, issue of September 10.
OCTOBER 12–17. Seventh International Congress of Pediatrics. Page 170, issue of July 23.
OCTOBER 13. New York Society for Circulatory Diseases. Page 506, issue of September 17.
OCTOBER 14. New England Cardiovascular Society. Notice above.
OCTOBER 15–17. Annual Course in Postgraduate Gastroenterology. Page 260, issue of August 6.
OCTOBER 16. New England Society of Anesthesiologists. Page 428, issue of September 3.
OCTOBER 17–20. American Association of Blood Banks. Page 1126, issue of June 25.
OCTOBER 19–30. New York Academy of Medicine. Page xvii, issue of June 11.
OCTOBER 21–23. International Symposium on Virus Infections. Notice above.
OCTOBER 23 and 24. Eastern Section of American Trudeau Society. Page 506, issue of September 17.
OCTOBER 25–29. American Institute of Dental Medicine. Page 124, issue of July 16.
OCTOBER 28. New England Obstetrical and Gynecological Society. Page 868, issue of November 27.
NOVEMBER 2–4. New England Postgraduate Assembly. Hotel Statler, Boston.
NOVEMBER 6 and 7. American College of Cardiology. Page 506, issue of September 17.
NOVEMBER 18. Massachusetts Society of Examining Physicians. Notice above.
NOVEMBER 19 and 20. Inter-Society Cytology Council. Page 170, issue of July 23.
DECEMBER 6. American Academy of Dental Medicine. Page 170, issue of July 23.
MAY 31–JUNE 3, 1954. American Urological Association. Page xvii, issue of July 23.
SEPTEMBER 12–15, 1954. Second International Congress of Cardiology. Page 44, issue of July 2.
SEPTEMBER 16–18, 1954. American Heart Association. Annual Scientific Sessions. Page 44, issue of July 2.

DISTRICT MEDICAL SOCIETIES

ESSEX NORTH
SEPTEMBER 30. Amesbury Country Club, Amesbury.

MIDDLESEX EAST
NOVEMBER 18.
JANUARY 20. (Combined with the Auxiliary.)
MARCH 24.
MAY 12. Annual Meeting. (Harlow Dinner.)

(*Notices concluded on page xi*)

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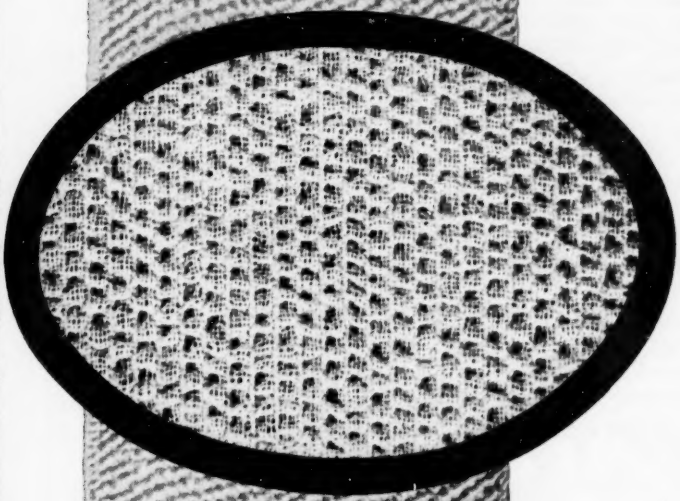

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NOTICES (*Concluded from page 546*)

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, OCTOBER 1

THURSDAY, OCTOBER 1

*8:30–10:00 a.m. Orthopedic Staff Conference. Boston City Hospital.
*9:00–10:00 a.m. Arthritis Grand Rounds. Robert Breck Brigham Hospital.
*9:00–10:00 a.m. Cardiac Grand Rounds. Main Amphitheater, Children's Medical Center.
*11:00 a.m.–12:30 p.m. Hand Clinic (Physical Medicine and Rehabilitation Service). Boston City Hospital.
*5:00–6:00 p.m. Surgical Division Meeting. Mount Auburn Hospital, Cambridge.

FRIDAY, OCTOBER 2

*10:00 a.m. Tuberculosis Surgical Clinic. South End Health Unit, 57 East Concord Street.
*10:00 a.m.–1:00 p.m. Medical and Surgical Grand Rounds. Drs. George W. Thorn and Francis D. Moore. Main Amphitheater, Peter Bent Brigham Hospital.
*10:30–11:15 a.m. Diabetes Lecture. Dr. Elliott P. Joslin. New England Deaconess Hospital.
*1:30 p.m. Fertility and Endocrine Clinic. Free Hospital for Women, Brookline.
*1:30 p.m. Tumor Clinic. Mount Auburn Hospital, Cambridge.
*4:00–10:00 p.m. Alcoholism Clinic. By appointment. Washingtonian Hospital, 41 Waltham Street.

SATURDAY, OCTOBER 3

*9:00 a.m. Proctology Clinic. Peter Bent Brigham Hospital.
*9:00 a.m. Alcoholism Clinic. Peter Bent Brigham Hospital.
*11:00 a.m.–12:00 m. Blood Clinic. Dr. William Dameshek, Stearns Auditorium, New England Center Hospital.

MONDAY, OCTOBER 5

*8:00–9:00 a.m. Combined Medical and Surgical Rounds for Diabetic Surgery Cases. New England Deaconess Hospital.
*8:30–9:30 a.m. Clinic by entire Surgical Staff and Anesthesia Staff. Cheever Amphitheater, Dowling Building, Boston City Hospital.
12:00 m. Clinicopathological Conference (Boston Floating Hospital). Pratt Lecture Hall, Joseph H. Pratt Diagnostic Hospital.
*12:15–1:15 p.m. Clinicopathological Conference. Main Amphitheater, Peter Bent Brigham Hospital.
5:00 p.m. Edward K. Dunham Lecture. Building D, Harvard Medical School.
*7:00–9:00 p.m. Anesthesia Teaching Conference. Stearns Auditorium, New England Center Hospital.

TUESDAY, OCTOBER 6

*9:00 a.m. Geriatrics Clinic. Peter Bent Brigham Hospital.
*12:00 m.–1:00 p.m. Pediatric Rounds. Burnham Memorial Hospital for Children, Massachusetts General Hospital.
*12:15–1:15 p.m. X-ray Conference. Dr. Merrill Sosman. Main Amphitheater, Peter Bent Brigham Hospital.
12:30–1:30 p.m. Medical Journal Club. Private Dining Room, New England Deaconess Hospital.
*5:00 p.m. Surgical Journal Review. Mount Auburn Hospital, Cambridge.
*5:00–6:00 p.m. Service Meeting followed by Clinical Conference (Medical, Surgical, Obstetrical). Faulkner Hospital.

WEDNESDAY, OCTOBER 7

*12:00 m. Boston State Hospital Psychiatric Seminar. Reception Building Auditorium, 591 Morton Street, Dorchester.
*12:00 m.–1:00 p.m. Medical Conference. (Children's Medical Center.) Jimmy Fund Building, 25 Binney Street.
*12:30 p.m. Weekly Pathological Meeting. Joslin Auditorium, New England Deaconess Hospital.
12:30–1:30 p.m. Weekly Staff Review of Autopsies. Dr. William A. Meissner. Joslin Auditorium, New England Deaconess Hospital.
*2:00–3:00 p.m. Pediatric Conference for Practitioners. (Children's Medical Center.) Jimmy Fund Building, 25 Binney Street.
*4:00 p.m. Thoracic Conference. Held by Overholt Clinic. Harris Hall, New England Deaconess Hospital.
4:00–5:30 p.m. Fracture Lecture. Boston City Hospital.
5:00 p.m. Edward K. Dunham Lecture. Building D, Harvard Medical School.

*Open to the medical profession.

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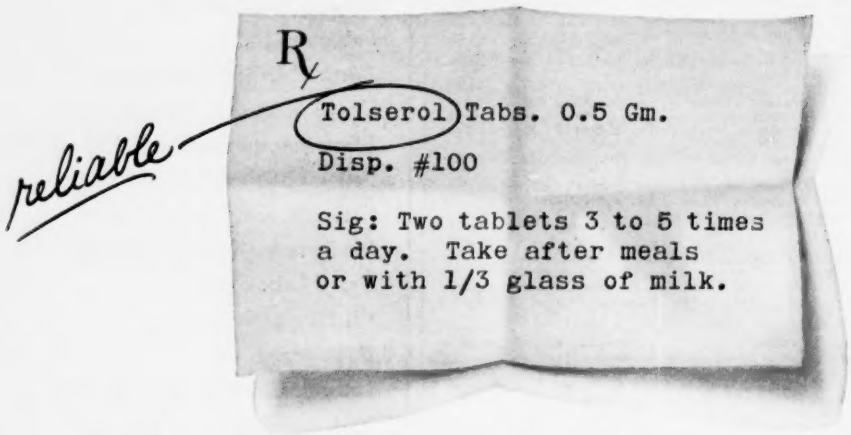

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